



THE  
Journal of Obstetrics & Gynaecology  
of the British Empire

VOL. 51, No. 1

NEW SERIES

FEBRUARY, 1944

The Incidence of Haemolytic Disease of the Foetus ("Erythroblastosis Foetalis") in Different Families. The Value of Serological Tests in Diagnosis and Prognosis.

(A Report to the Medical Research Council from the S.W. London Blood Supply Depot.)

BY

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It is now generally accepted that the disease Erythroblastosis Foetalis, better called Haemolytic Disease of the Foetus (or New-born) is caused by the action on the foetal erythrocytes of immune agglutinins formed in the mother's serum during pregnancy and passed through the placenta into the foetal circulation. Levine and his co-workers (Levine and Stetson<sup>1</sup>; Levine *et al.*<sup>2</sup>) first brought forward evidence to show that the formation of these agglutinins is stimulated by an antigen present in the foetal red cells but absent from the maternal red cells, the antigen having been inherited from the father, and they demonstrated that the Rh agglutinin must be the antigen responsible in a very large proportion of the cases. For whereas the blood of only 15 per cent of subjects taken at random was found to be Rh negative (i.e. the erythrocytes lacked the Rh agglutinin), among the mothers of infants affected with haemolytic disease, as many as 93 per cent were Rh negative, whereas all the infants and fathers tested were Rh positive. It was, therefore, concluded that the destruction of the foetal erythrocytes (Rh positive) was

caused by the formation of anti-Rh agglutinins in the serum of the mother (Rh negative). Confirmatory observations have been published by Wiener<sup>3</sup> and by Boorman, Dodd and Mollison.<sup>4</sup>

A great deal more remains to be learnt about the whole process, however. For instance, although the combination Rh positive infant and Rh negative mother occurs in 9.46 per cent of all pregnancies (Haldane<sup>5</sup>), it seems clear that the infant is affected with haemolytic disease in only a small proportion of these cases for the incidence of haemolytic disease is only one in 400 or 0.25 per cent of all pregnancies. For this reason the mere demonstration that the mother is Rh negative and the infant Rh positive, cannot by itself be regarded as satisfactory diagnostic evidence of haemolytic disease of the foetus. Moreover, since the mother is Rh positive in a small proportion of cases in which the infant is affected with this disease, such a finding will not serve to exclude the diagnosis.

It is hoped that an analysis of the results obtained from serological tests made on a

large series of families may help in the assessment of the value of these tests in diagnosis and prognosis.

### METHODS.

One hundred\* families were tested because of the birth of a foetus suspected of being affected with haemolytic disease. In every case the mother was tested and in the majority of cases the infant or father was also examined. In many families one or more of the previous siblings were also tested. In another 70 cases tests were made on women who had given birth to one or more stillborn foetuses; and in a further 60 cases in which the infant was thought to be affected with "physiological jaundice" mother and infant were tested. A group of normal mothers and infants were also tested to obtain control material.

The ABO group of the erythrocytes was determined by a tube method and the Rh group was determined by the technique described previously (Boorman, Dodd and Mollison<sup>1</sup>), using 3 different human immune anti-Rh sera. No attempt was made to differentiate between subgroups of Rh. Usually the erythrocytes of a given family were tested against the same anti-Rh sera and in many instances they were tested directly against the mother's serum. The mother's serum was almost always tested against the same 2 Rh positive bloods and against 2 Rh negative bloods. The Rh positive bloods included one blood which was known to give consistently strong reactions with many different human anti-Rh sera; the other Rh positive blood used gave weaker reactions with most anti-Rh sera but with occasional sera gave even better reactions than the first blood. This second blood was chosen for routine tests because it appeared to be qualitatively

different from the first blood and because its reactions seemed typical of the majority of Rh positive bloods. [Since this work was completed, the classification of the subgroups of Rh has advanced considerably. The first blood referred to has been tested and found to belong to subgroup Rh<sub>2</sub> (see Wiener<sup>2</sup>) whereas the second blood belongs to subgroup Rh<sub>1</sub> (genotype, Rh<sub>1</sub> Rh<sub>1</sub>; see Race and Taylor<sup>3</sup>).]

When anti-Rh agglutinins were found, the serum was titrated against the same test cells at intervals after delivery as the opportunity occurred.

In cases in which anti-Rh agglutinins were not found in the mother's serum, the serum was tested against 20 different group (O) bloods taken at random, to discover whether any atypical agglutinins were present. In all these cases in which anti-Rh agglutinins were not found, and in many of those in which anti-Rh agglutinins were found, the anti-A and anti-B agglutinins (if present) were titrated at various intervals after delivery.

The technique employed for estimating the titre of anti-A and anti-B agglutinins was that described Aubert *et al.*<sup>4</sup> For the titration of anti-Rh agglutinins the method was modified, firstly, by placing the tubes in the incubator for at least 2 hours instead of allowing them to stand at room temperature, and secondly, by handling the tubes gently so as to avoid breaking up the agglutinates. It should be noted that in any titration technique in which one pipette is used to make serial dilutions, a certain degree of "carry-over" is inevitable and therefore the recorded titre will be higher than the true value. (The titre of a serum is usually expressed as the reciprocal of the highest dilution in which agglutination occurs). However, in most cases only comparative and not absolute titration values are required, so that the use of one pipette is no disadvantage.

\* Serological findings of 48 of these families have been reported previously (Boorman, Dodd and Mollison, 1942).

In approximately two-thirds of the cases the mother was tested within 20 days of the birth of an affected infant and in many of these repeated titrations of the serum were carried out during the 20 days after delivery. In the cases not tested within 20 days of birth, the tests were usually made within 3 months of delivery, but occasionally were not made until a year or more later.

In a few cases the patient's serum was examined at intervals during pregnancy.

### DIAGNOSTIC CRITERIA.

In assembling a series of families in which cases of haemolytic disease of the foetus are thought to have occurred, considerable difficulties are encountered because uncertainty quite often exists with regard to the diagnosis.

The diagnosis of haemolytic disease of the newborn can usually be established with reasonable certainty if the infant is seen at the time of the illness and its blood is examined. It quite often happens, however, that no blood examination is made and if the infant recovers and is seen for the first time at a later date it is often difficult to say, on clinical grounds alone, whether it was ever affected with the disease. In the case of stillborn foetuses, these difficulties become greater. Often no thorough pathological investigations are made or, in the case of macerated foetuses, are practicable. Even when sections of the tissues are prepared there may be difficulty in getting agreement from pathologists as to the significance of a certain degree of erythroblastosis in the organs.

There is a tendency, therefore, to select the material according to the results of the serological tests. When the mother is found to have become sensitized to the Rh agglutinin, the case is said to be one of haemolytic disease of the foetus, but when the serological findings are different, this

diagnosis is rejected. This method of selection is obviously undesirable. For it will leave out of account the cases in which the disease is due to sensitization of the mother to the Rh agglutinin but, owing to the time of examination or some other factor, anti-Rh agglutinins cannot be detected in the serum. Moreover, this selection will lead to the omission of cases in which the disease is due to sensitization of the mother to some antigen other than Rh.

In an investigation of the serological findings in cases of haemolytic disease it seems desirable to adopt definite clinical and pathological criteria for the diagnosis of the condition and then to analyse the serological results in "proved" cases. When this first assessment has been made, however, and some idea has been gained of the serological findings in a series of proved cases, it is desirable to take the further step of examining the serological findings in a series of doubtful cases and to discover what clinical and pathological findings accompany them.

In the present paper the above order has been followed. The clinical and pathological criteria adopted for the diagnosis of haemolytic disease were as follows:

1. "*Hydrops Foetalis*." Hydrops of the foetus, with anaemia and erythroblastæmia if born alive, or with evidence of erythroblastosis of the organs if stillborn. An oedematous foetus exhibiting ascites has not been considered a proved case of haemolytic disease of the foetus in the absence of haematological or pathological evidence.

2. "*Stillbirth of the Foetus without Hydrops*." One family has been included because of the birth of a stillborn foetus which showed widespread extramedullary erythropoiesis.

Stillbirths occurred in many other families but in these families one or more cases satisfying criteria (1), (3), or (4) also occurred and the families have been included on account of the occurrence of these latter cases.

3. "*Icterus Gravis Neonatorum*." Onset of jaundice in an infant within 3 days of birth, fol-



TABLE II.

*Some Examples of Families in which the Birth of at least Two Normal Infants  
Preceded the Birth of an Infant Affected with Haemolytic Disease.*

Family serial No.	Serological findings, Mother		Siblings: Year of birth, clinical condition and serological findings					
	Erythro- cytes	Serum	1	2	3	4	5	6
13	ORh-	Anti-Rh	1931 N ORh+	1933 N ORh+	1935 S.B. jaundiced ORh+	1937 jaundiced ORh+	1940 I.G. died	1942 S.B. oedematous
17	ORh-	Anti-Rh	1938 N ORh+	1940 N ORh+	1942 I.G. recovered ARh+			
25	ARh-	Anti-Rh	1939 N	1940 N	1942 twins I.G. both died, both ARh+			
11	ORh-	Anti-Rh	1929 N ORh+	1931 N ORh-	1936 N ORh-	1938 N ORh+	1940 N ORh+	1942 I.G. recovered ORh+
29	ORh-	Anti-Rh	1928 N died later	1930 N ORh-	1934 N ARh-	1938 N ARh+	1942 I.G. recovered ARh+	
37	ARh-	Anti-Rh	1934 N	1936 N	1940 I.G. recovered (kern- icterus) ORh+			
47	ARh-	Anti-Rh	1921 N  1933 I.G. died	1922 N  1934 S.B. 9/12	1924 N  1936 S.B. 7/12	1926 N  1942 S.B. 9/12	1928 N	1931 I.G. died
43	ARh-	Anti-Rh	1923 N  1942 I.G. recovered ORh+	1925 N ARh+	1927 N ORh+	1929 N Rh+	1931 N ARh+	1933 N ORh+
45	ORh-	Anti-Rh	1940 N ORh+	1941 N twins (ORh+ ARh+)	1942 I.G. recovered ORh+			

TABLE II. (Continued).

Family serial No.	Serological findings, Mother		Siblings: Year of birth, clinical condition and serological findings					
	Erythrocytes	Serum	1	2	3	4	5	6
51	ARh-	Anti-Rh	1931 N	1931 N	1931 S.B. 5/12	1939 H.A. recovered	1942 S.B.	
51	ORh-	Anti-Rh	1935 N	1937 N	1939 I.G. died	1942 I.G. recovered ORh+		
70	ARh-	Anti-Rh	1931 N died later	1937 N ARh+	1913 I.G. recovered ARh+			
75	ARh-	Anti-Rh	1931 N	1937 N	1943 I.G. recovered ARh+			
61	ARh	Anti-Rh	1931 N	1933 N	1935 N	1937 N	1939 jaundiced recovered	1913 I.G. recovered ARh+

of an infant which, although affected, recovered. Again, in family 90 the birth of 3 infants, all of whom died of icterus gravis within a few days of birth, was followed by the birth of an infant which, although affected with icterus gravis, recovered spontaneously. The next infant, however, died of icterus gravis within a few days of birth. It is worth mentioning that in this family it was at first reported that the 3rd child which recovered had always been perfectly normal. Only when the mother was directly questioned did it emerge that the 3rd child had been seriously jaundiced from the 1st day of life for many weeks and had only recovered after a critical illness. This illustrates quite well the difficulty which is experienced in obtaining reliable information about these families.

In 17 families the 1st pregnancy ended in a miscarriage or stillbirth or in the birth

of an infant which died within 24 hours of delivery. In only 4 of these 17 cases could the cause of death be definitely ascribed to haemolytic disease according to the criteria mentioned above. Some details of these 4 cases are given in Table IV. Of the remaining 13 cases in which the cause of death of the firstborn infant could not be determined, the histories were as follows: miscarriages during the first 6 months of pregnancy: 5 cases; stillbirths during the last 3 months of pregnancy: 5 cases; death within 24 hours of delivery: 3 cases. In 6 other families the firstborn infant was affected with haemolytic disease but recovered. Details of these families are also given in Table IV.

Thirty normal siblings (including the 13 firstborn infants mentioned above), born prior to the birth of an affected infant, were tested. Of these 26 were Rh positive and 4 Rh negative.

TABLE III.

*Some Examples of Families in which the Birth of a Normal Infant Followed the Birth of One or More Infants Affected with Haemolytic Disease (According to Certain Defined Criteria).*

Family serial No.	Serological findings, Mother		Siblings: Year of birth, clinical condition and serological findings						
	Erythrocytes	Serum	1	2	3	4	5	6	7
35	ORh—	Anti-Rh	1937 N ORh+	1939 I.G. died	1941 N ARh—	1942 N ARh—			
41	ARh—	Anti-Rh	1922 N	1927 N	1933 N ARh+	1938 N	1939 I.G. died	1941 N ARh—	1942 N ORh—
63	ARh—	Anti-Rh	1926 Misc. 4½ mths.	1927 I.G. died	1930 N ARh—	1942 I.G. recovered ARh+			
83	ORh—	Anti-Rh	N	I.G. Kern- icterus	N ORh—				

N.B.—Family 60, in which the birth of an infant who died of "icterus gravis" was followed by the birth of an infant which was mildly jaundiced and recovered, is not included in this table because there was some doubt as to whether this latter infant was or was not affected with haemolytic disease.

In 5 families the birth of an affected infant was followed by the birth of one or more normal children. In 4 families the normal children tested were all found to be Rh negative. In the fifth family, the normal child was Rh positive. It must be added, however, that in this case there was a suspicion that the infant was very mildly affected with haemolytic disease.

(d) *Changes in Titre of Immune Anti-Rh Agglutinins during Pregnancy and after delivery.*

In 7 cases a mother who had previously given birth to an infant known to have been, or thought to have been affected with haemolytic disease, was tested repeatedly during a subsequent pregnancy. In every instance anti-Rh agglutinins were found in her serum. In 2 of the 7 cases a progressive increase in titre was noted during pregnancy, and in both of these an affected

infant was subsequently born. In 3 other cases an affected infant was subsequently born but no change in the titre of the anti-Rh agglutinins was detected. In the remaining 2 cases there was no change in the titre of the anti-Rh agglutinins and the infant, when born, proved to be Rh negative and unaffected. Evidently the formation of anti-Rh agglutinins in the mother's serum in these cases had been stimulated by a previous pregnancy in which an Rh positive infant had been carried.

In the great majority of the 100 cases some increase in titre of anti-Rh agglutinins was observed *following* the birth of an Rh positive affected foetus and the peak of this response was attained between the 8th and 20th days after delivery in almost every case. (Details of these and other immune responses in connexion with pregnancy are being published elsewhere).

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## PART IV.

*Some Examples of Foetuses in which the Parturient Infant was Affected with Haemolytic Disease (According to Certain Defined Criteria).*

Family serial No.	Parents		Child	Child's Year of birth, clinical condition, and pathological findings			Notes
	Mother	Father		1	2	3	
50	ARh+	Anti-B+	ORh+	1942 H.D., recovered ARh+			
51	ARh+	Anti-B+	ARh+	1942 I.G. died			
52	ARh+	Anti-B+		1943 I.G. died	1946 H.D. died	1948 H.D. died	
53	ORh+	Anti-B+	ARh+	1942 I.G. recovered ARh+			
54	ARh+	Anti-B+		1942 I.G., recovered ORh+			
55	ORh+	Anti-B+		1942 I.G. recovered ORh+			
56	BRh+	No Anti-Rh	ORh+	I.G. died I.G. recovered BRh+	I.G. died I.G. died	I.G. died	
57	ORh+	No Anti-Rh Immune Anti-A		1942 H.A., recovered ARh+			Immune anti-A; titre 8,000 at peak
58	ARh+	Immune Anti-B	BRh+	1942 I.G., died			Immune anti-B; titre 32,000 at peak
59	ORh+	Immune Anti-B	BRh+	1942 I.G., recovered BRh+			Immune anti-B; titre 8,000,000 at peak

## DISCUSSION OF SEROLOGICAL FINDINGS.

*Findings of anti-Rh agglutinins in sera of Rh negative mothers.*

It was mentioned above that Levine, Katzin, Vogel and Burnham,<sup>7</sup> only found

anti-Rh agglutinins in the sera of a proportion of Rh negative women whose infants were affected with haemolytic disease of the foetus. Of 141 such mothers, anti-Rh agglutinins were found in the sera of 41

Among 70 cases who were examined within 2 months of delivery, however, the proportion was much higher, i.e. 33 out of 70. Wiener<sup>6</sup> also has stated "in more than half the cases anti-Rh antibodies are not detectable" and has supported this statement with the reference "unpublished observations." It will be evident that the experience recorded in this paper is considerably different since anti-Rh agglutinins were found in 93 out of the 97 Rh negative mothers tested. This may be due in part to the fact that many of the present cases were examined within a short time of delivery. On the other hand, among 37 cases examined at 2 months or later after delivery, all but 1 still had detectable anti-Rh agglutinins. It must therefore be concluded that the technique used in the present tests was more sensitive than that employed by the authors referred to above. In this connection it is of interest that Race, Taylor, Cappell and McFarlane<sup>7</sup> who used a technique almost identical with ours, also found that a high proportion of the sera of Rh negative women, whose infants were affected with haemolytic disease, contained anti-Rh agglutinins; (they were demonstrated in 38 out of 44 sera, many of which were not examined for some months or more after delivery).

The observation of this high incidence of anti-Rh agglutinins in the sera of Rh negative mothers whose infants are affected with haemolytic disease suggests that, provided the mother's serum has been examined within say, 20 days of delivery, and a sensitive technique has been used for the examination, failure to find anti-Rh agglutinins in the serum of an Rh negative mother should be interpreted as meaning that her infant is probably not affected with haemolytic disease.

As mentioned above, in one family, mother, father and infant were all Rh positive, but the mother's serum agglutinated

the erythrocytes of the infant and father and also approximately 1 in 3 Rh positive bloods (groups O and A) taken at random. It was observed that the serum only agglutinated 2 out of 45 Rh negative bloods. Subsequently, it was possible to identify this agglutinin as anti-Rh<sub>2</sub> (Wiener and Sonn<sup>10</sup>); fuller details of its reactions are given by Race, Taylor, Boorman and Dodd<sup>7</sup> in a note in which the serum is described as *K*. The fact that this agglutinin was responsible for the destruction of the foetal erythrocytes was demonstrated by transfusing the infant with a mixture of 2 bloods, one of which was agglutinated by the mother's serum and the other of which was not. It was found that the "incompatible" erythrocytes were far more rapidly destroyed in the infant's circulation than were the "compatible" erythrocytes (Mollison.<sup>11</sup>)

In 2 families, the mother's serum was found to contain potent anti-B agglutinins incompatible with the foetal erythrocytes, the titre of the agglutinins being 32,000 and 8,000,000 respectively. It seems probable that the affection of the infant in these cases was caused by these immune agglutinins (see discussion below).

#### SUMMARY OF FINDINGS IN 100 PROVED CASES OF HAEMOLYTIC DISEASE OF THE FOETUS.

Immune agglutinins, incompatible with the foetal erythrocytes were found in 96 out of the 100 cases. In 93 cases the agglutinin was anti-Rh; in one other case, the agglutinin was identified as anti-Rh<sub>2</sub> and in the remaining 2 cases it was anti-B. In the latter 2 cases the potency of the agglutinins was far greater than that observed in the majority of cases in a series in which the infant was normal. In the following section, therefore, the finding of immune agglutinins of these kinds, incompatible

with the foetal erythrocytes has been taken as highly suggestive evidence that the foetus was affected with haemolytic disease.

It is realized that this method of selection may lead to the exclusion of some genuine cases for, as mentioned above, anti-Rh agglutinins are not always found in the sera of Rh negative mothers whose infants are affected with haemolytic disease, even when the time of examination is favourable. When the mother's serum is examined many months or years after delivery, immune agglutinins will often have disappeared and serological tests are then incapable of affording decisive evidence of previous iso-immunization. Few such cases, however, have been included and the great majority were examined within a short time of delivery.

#### II. CASES OF STILLBIRTH OR NEONATAL DEATH (WITHIN 48 HOURS OF DELIVERY) IN FAMILIES IN WHICH NO PROVED CASE OF HAEMOLYTIC DISEASE OCCURRED.

Seventy mothers who had had one or more miscarriages or stillbirths were tested. In 11 cases anti-Rh agglutinins were found in the serum; on the basis of the results in Section I, the death of the foetus in these 11 cases is considered to have been due to haemolytic disease. In three other cases, very potent anti-A or anti-B agglutinins were found (peak titres 500,000, 1,000,000 and 32,000). It is considered uncertain whether or not these foetuses were affected with haemolytic disease (see discussion below).

The failure to find immune agglutinins in the remaining 56 cases renders it unlikely that in more than a few of these instances (at the most) was the foetus affected with haemolytic disease, since the great majority of these cases were examined within 20 days of delivery. This conclusion receives further support from the observation that only 6 of these 56 mothers were Rh nega-

tive. In the case of one of the 6 Rh negative mothers, iso-immunization may have occurred, but since the serum was not examined until 5 years after the last delivery a definite opinion could not be given. The other 5 Rh negative mothers were tested within 14 days of delivery.

Some details of the 11 families in which the stillbirth or miscarriage was apparently attributable to iso-immunization are given in Table V. It will be noted that in 5 of the cases the diagnosis of "hydrops foetalis" had been made from the appearance of the foetus. In these cases, however, no pathological examination was carried out and according to the criteria adopted these cases could not therefore be included as "proved instances of haemolytic disease of the foetus" in section I. In the remaining 6 families oedema of the foetus was not recorded and the infant was macerated or outwardly normal. In this group of 11 cases, the dead foetus was born at the 7th month of pregnancy in all but one instance. In this latter instance (family 84) a stillbirth at 7½ months of pregnancy was followed by miscarriages at 5½ months and 3½ months respectively.

Among the group of 56 cases in which the stillbirth or miscarriage did not appear to be due to haemolytic disease, the birth of the dead foetus occurred in many of the cases at an early stage in pregnancy (i.e. within the first 6 months). In some, however, the birth occurred at a late stage and in a few the diagnosis of hydrops foetalis was considered on clinical grounds. The following case may be quoted as an example: First 2 pregnancies, normal infants; 3rd pregnancy, macerated foetus exhibiting gross ascites delivered at term. An examination of the blood or tissues was not carried out, but serological tests showed that the mother and foetus were both group O, Rh positive and no incompatibility could be detected between the

TABLE V.

*Some Examples of Families in which More than One Stillbirth (or Miscarriage) occurred and in which the Serological Findings suggested that the Foetal Death was due to Haemolytic Disease.*

Family serial No.	Serological findings, Mother		Siblings: Clinical condition and serological findings			
	Erythrocytes	Serum	1	2	3	4
21	ARh -	Anti-Rh	N	N	S.B.*	
22	ORh -	Anti-Rh	N, ORh+	S.B.	S.B.*	
26	ORh -	Anti-Rh	N	S.B., 7/12	S.B., 8/12	
33	ARh -	Anti-Rh	N S.B.	N N	N S.B.*	N
50	ARh -	Anti-Rh	S.B., F.T.			
57	ARh -	Anti-Rh	N	died at 12 hrs.	S.B., F.T.	
58	ARh -	Anti-Rh	N	S.B.*		
82	ORh -	Anti-Rh	S.B.	died 1st day		
84	ARh -	Anti-Rh	S.B., 7 $\frac{1}{2}$ /12	S.B., 5 $\frac{1}{2}$ /12	S.B., 3 $\frac{1}{2}$ /12	
92	ARh -	Anti-Rh	N	S.B.*		
94	ARh	Anti-Rh	N	S.B., 7/12	S.B.*	

\* Clinical diagnosis "Hydrops foetalis."  
F.T. = Full Term.

mother's serum and the infant's erythrocytes. Moreover, the mother's serum, when examined again 10 days after delivery, did not show any evidence of atypical agglutinins. It therefore appeared unlikely that the foetus was affected with haemolytic disease.

### Discussion.

In 59 out of 70 cases in which a mother had given birth to one or more stillborn foetuses, or had miscarried on one or more occasions, no evidence of iso-immunization to the Rh factor could be obtained. In the remaining 11 cases, on the other hand, there seemed little doubt that the death of the foetus was due to haemolytic disease, for iso-immunization of the mother to the Rh agglutinin was demonstrated.

Although on the whole the cases of foetal

death due to haemolytic disease occurred late in pregnancy, and the cases not attributable to haemolytic disease were mostly miscarriages during the early months of pregnancy, the history alone is an unreliable guide in the individual case, since exceptions to both these rules occur. Among some of the 59 cases in which evidence of iso-immunization to the Rh factor was not obtained, death of the foetus occurred at the 7th or 8th month of pregnancy in several instances. Conversely, in one family included in Section I (see Table I), a mother gave birth at the 5th month to a stillborn foetus which exhibited the typical features of hydrops foetalis. (We are indebted to Dr. J. R. Gilmour for this opinion. He found lipoid infiltration of the suprarenal cortex and points out that this change only occurs in hydrops foetalis).

Serological tests are likely to prove valuable in deciding in a given case whether or not foetal death is attributable to haemolytic disease.

### III. SEROLOGICAL TESTS IN CASES IN WHICH THE INFANT WAS APPARENTLY NORMAL.

Sixty infants developing "physiological jaundice" were tested, together with their mothers. Any infant developing jaundice within the first 5 days of life was considered to be affected with "physiological jaundice," provided that there were none of the classical features of "icterus gravis" as defined above, and provided that there was reasonable evidence that the jaundice was not caused by syphilis, sepsis or congenital obliteration of the bile ducts.

#### *Rh Group Differences.*

Six of the 60 mothers were Rh negative. In 3 of these cases, anti-Rh agglutinins were found in the mother's serum (all 6 cases were tested repeatedly during the 20 days following delivery). One of these 3 cases occurred in a family described above (see Table II) in which a previous infant had been affected with "icterus gravis." The present infant may also have been affected (though mildly) with haemolytic disease because its haemoglobin value was only 92 per cent 8 days after delivery and a blood film made on the 3rd day of life showed as many as 15 nucleated red cells per 100 leukocytes. Unfortunately, the child could not be examined again after the 8th day. However, it is known that it was perfectly healthy at the 3rd month of life so that it cannot have been very seriously affected. In the other 2 cases the infant only developed the mildest degree of jaundice and repeated examination of blood films never revealed any abnormality so that the diagnosis of haemolytic disease appeared to be definitely excluded and the

jaundice of the infant could not reasonably be ascribed to this cause.

#### *ABO Group Differences.*

Among the first 25 cases tested, the mother's serum was found to be incompatible with the infant's erythrocytes with respect to the anti-A and anti-B agglutinins in as many as 13 cases. Since the expected incidence of this kind of incompatibility (i.e. due to anti-A or anti-B agglutinins) is only one in 5 births (according to a figure kindly supplied by Dr. G. L. Taylor), it was thought that this finding was suggestive of some relationship and that some cases of physiological jaundice might in fact be mild cases of haemolytic disease of the newborn due to destruction of the foetal erythrocytes by anti-A or anti-B agglutinins (see Boorman, Dodd and Mollison').

In the next 32 consecutive cases tested, however (excluding the 3 cases in which anti-Rh agglutinins were found in the mother's serum), the incidence of this kind of incompatibility was only 7, almost exactly the expected figure in a random sample of cases. Thus in the majority of cases of "physiological jaundice" no incompatibility between the mother's serum and the infant's erythrocytes could be detected.

Further evidence was obtained from another group of cases in which routine tests were made on the bloods of mothers and infants taken at random. In 26 cases in which the mother's serum was incompatible with the foetal erythrocytes, the infant did not develop severe jaundice in a single case and developed mild transient jaundice in only a small number of instances. In 16 out of these 26 cases there was evidence of an immune response following the birth of a child, the highest titres attained falling between 256 and 11,000.



cortical striations were moderately diminished and the glomerular tufts scarcely visible. The little tumors were gray inside. The left kidney weighed 195 Gm. In the fat close to its dorsal surface and convex margin was a firm tumor 12 mm in diameter, pearly white inside. In the lower pole was a nodule of white and faintly yellow tumor tissue 28 by 22 by 28 mm, extending through the cortex into a renal pyramid. On the ventral surface near the convex margin embedded deeply in the cortex was another 1 cm in diameter. In other respects this kidney was like the right.

In the cortex of the upper pole of the left suprarenal gland was a gray tumor nodule 3 mm in diameter. In the fat at the upper pole were two others, one 3 and the other 6 mm in diameter. There was a moderate diminution of the yellow substance of the cortex. The lining of the suprarenal vein was smooth throughout.

In the outer part of the upper margin of the left innominate bone and its ala was a tumor 13 cm along the iliac crest, 5 cm wide and extending into the ala 5.5 cm. It was surrounded by a fibrous capsule and was very soft. The bone was destroyed for a depth of 5.5 cm, but just beneath the capsule were spicules of bone. The tissue was gray to yellow, except for minute places that contained a yellow fluid. Approximately 20 per cent of surfaces made by cutting consisted of these necrotic regions. The muscle about the bone seemed to be pushed away rather than invaded by tumor tissue.

The seventh thoracic intervertebral disk was thickened by a mass of gray-pink, moderately firm tissue which projected against the dura of the cord. This thickened tissue was roughly wedge-shaped, the widest place being along the cord, where it was 1.8 cm, from here it tapered forward. The intervertebral disk left white surfaces when lifted from the bodies of the seventh and eighth thoracic vertebrae, but in the cartilage were fine spicules of bone.

In the ninth rib, 3 cm from the anterior axillary line, was an erosion of the bone and a replacement by gray-white tissue, forming a nodule 3 cm long, 2 cm wide and 1.6 cm thick. On the left side in the body of the eleventh thoracic vertebra, just above the margin of the twelfth rib, was a pink-gray mass 2 cm long, measured along the spinal column, 1.5 cm wide and projecting about 5 mm. This extended about 5 mm into the substance of the bone, and forward about the same distance. The bone was eroded and replaced by a soft gray tissue. There were no gross changes in the heart, liver, spleen, pancreas, gall-bladder, stomach, intestines, trachea, esophagus, large blood vessels, thyroid gland, testes, epididymides, prostate gland, seminal vesicles, appendix vermiformis, brain or leptomeninges, except as stated.

*Histology*—In sections from the wall of the bronchus in the upper lobe of the left lung from which the tumor radiated,<sup>1</sup> from many parts of the tumor farther out in the lung, and from the various metastatic growths in the kidney, suprarenal gland, eleventh rib and left innominate bone, the tumor cells were alike, tall cylindric cells arranged in tubules or solid cords (fig 3), much like the formations in cylindric cell carcinomas of the colon, but without much production of mucin. They were undoubtedly from the glands in the mucous membrane of the bronchus, from which the tumor grew so symmetrically. In the nodules in the kidney the tumor cells were more compact, and in some of the sections from the tumor of the lung there was a large amount of necrosis.

1 Kaufmann. Lehrbuch der speziellen pathologischen Anatomie 1 312, 1911 (The author refers to the bronchus from which the tumor arises as a pedicle for the tumor.)

The short duration of the illness, the discovery of a tumor in the thorax, the suspicion that the tumor of the innominate bone was primary and followed an injury, and the character of the tumor a cylindric cell carcinoma, are the conspicuous features of this second bronchiogenic tumor.

The next tumor, reported with permission of Dr. H. B. Thomas, also from St. Luke's Hospital, was of much longer duration and remained unrecognized until shortly before the patient's death. It also arose from glands in the mucous lining of a bronchus.



Fig. 3—Photomicrograph of the metastatic tumor of the left innominate bone (tumor number 2). *A* indicates collagen fibers (periosteum).

CASE 3—*History*—I. G., a man aged 38, was admitted to the hospital on May 21, 1925, complaining of pain in the right forearm, index and middle fingers which began insidiously about one year before admission. During February, 1925, a graft of fascia lata was transplanted about the right ulnar nerve. The right forearm was swollen, from the elbow to the wrist and fingers with induration about the elbow and marked tenderness. The temperature was 98.4 F. the pulse rate was 88, the respirations, 18. Mucositis and osteomyelitis of the right radius and ulna were diagnosed. Necrotic bone was removed June 1, 1925. During the operation the bones were enlarged, and the bone tissue was sclerotic changes that suggest syphilis. Microscopically the tissues contained regions of chronic inflammation and fibrous tissue replacement of the fat in the marrow spaces. There was no change in the hemoglobin or in the number of cells in the blood. White cell counts and tests of the blood and spinal fluid were negative. No organisms were found.

in the pus, and nothing grew from it on culture medium. On July 26, 1925, the elbow was incompletely ankylosed at 90 degrees, swollen, tender and red, but the patient was not acutely ill. Examination of material from the head of the ulna and radius removed at operation Aug 13, 1925, indicated simply a low grade suppurative osteitis. The symptoms persisted. The urine never contained more than a trace of albumin. The Wassermann tests continued to be negative, the white cell count averaged about 9,800, the temperature was 98 F, the pulse rate, 104, and respirations, 22. By Oct 14, 1925, the entire arm was swollen again and was exceedingly painful. There were palpable lymph glands in the axilla, and five days later the arm was blue and edematous. It was amputated at the distal end of the proximal third of the humerus on October 24, and the

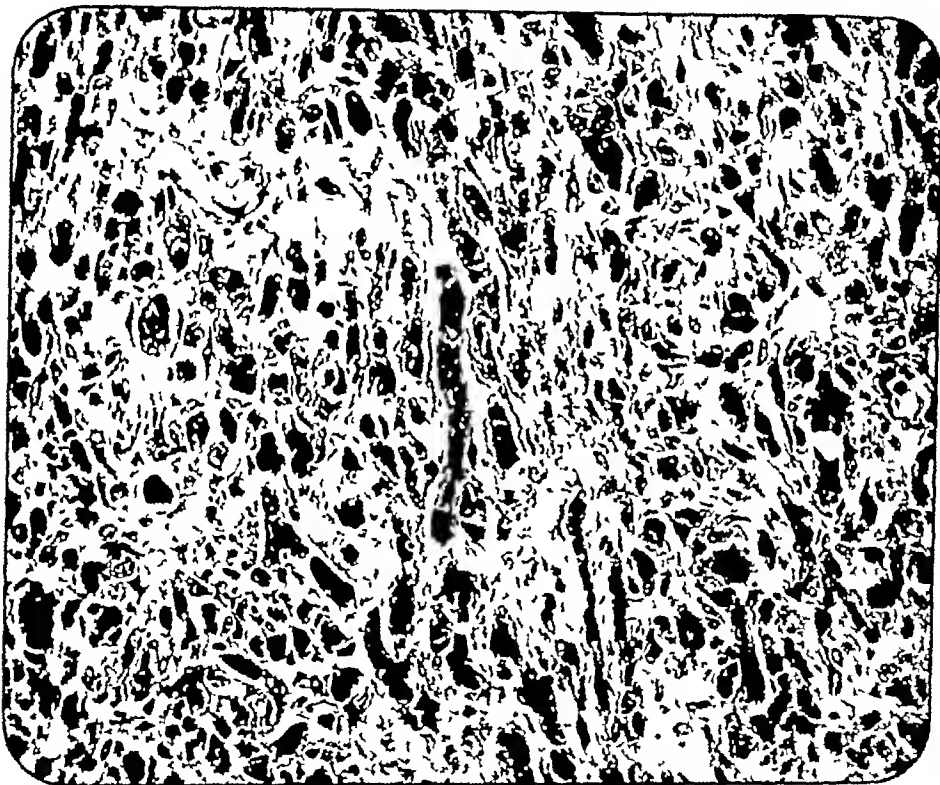


Fig 4—Photomicrograph of tumor cells discovered in tissues following surgical amputation of the arm (tumor number 3). The rows of epithelial cells are arranged in scar tissue like any so-called scirrhous carcinoma originating in a gland. At several clinical conferences, and by some pathologists to whom microscopic preparations were submitted, this tumor was diagnosed endothelioma.

patient was discharged on November 7, with a diagnosis of chronic periostitis of the bones of the right arm. Other diagnoses considered were hypertrophic osteoarthropathy of Marie, proliferating ossifying periostitis, condensing osteomyelitis and secondary hypertrophic osteitis.

*Histology*—In sections from a number of places in and around a callus where the several operations were made about the elbow, there was a great deal of scar tissue in the soft tissues enclosing irregular cells in poorly defined rows (fig 4). In many places the scar tissue greatly exceeded the cells, which were isolated

Some were necrotic, many were multinucleated, and some contained blood pigment. It was evident that cicatrization had hampered their growth. Prolonged search was necessary to find any indication of mitosis. In the section containing bone a great majority of the cells were single or in groups of two or three and separated from the stroma by small empty spaces. In larger groups however there was a faint but definite grouping simulating tubules. These conditions led to the conclusion that the cells were epithelial, and that the disease was caused by carcinoma dissemination. A primary pulmonary carcinoma was suspected. The patient was again thoroughly examined following this report, but the primary tumor was not found. He was readmitted to the hospital on Dec. 1, 1925 with pain in the right side and back for twenty-eight days, pain in the right side of the chest, more noticeable on inspiration and expiration, pain in the left wrist, both ankles and knees, and swelling of the ankles, knees and hand. The pain was continuous but never severe, and had been present since the amputation. The left hand was swollen and hard, but not edematous. The ulna and radius were rough, but not thickened. The feet were swollen and there was decreased resonance with fine rales over both apices. There was slight tenderness on pressure in the left sixth, seventh and eighth interspaces near the spine. Roentgen-ray examination showed a rarefaction and regions of condensation of the clavicles especially of the peristernum. The left half of the diaphragm was elevated and there was a left diaphragmatic pleuritis, but no tumors. The white cell count gradually increased to 14,200 on Dec. 26, 1925. The basal metabolic rate increased from plus 9.6 on Jan. 19, 1925, to plus 39.2 on Dec. 4, 1925. On December 2, there was selective dulness over both bases and tenderness near the spine. On the sixth, seventh and eighth vertebrae. There was no indication of any organic change in the central nervous system, and no evidence of tumor of the prostate gland. On December 18, a hypostatic pneumonia was found, and the temperature rose to 102 F., the pulse rate was 120 and respiration 44. The patient died on Jan. 1, 1926.

*Anatomic Diagnosis*—The following diagnosis was made: small primary carcinoma of the left bronchus, multiple metastatic carcinomas of the pleura, tracheobronchial and periaortic lymph glands, lungs, diaphragm and bone. Marked bilateral serofibrinous pleuritis, acute catarrhal tracheitis and bronchitis. Fibrinous changes in the leaflets of the mitral and aortic valves, moderate hyperplasia of the spleen, chronic diffuse nephritis, hyperemia of the urinary bladder and rectum, generalized senile arteriosclerosis, healing impaction stump of the right arm, old laparotomy scar, appendectomy scar of the cecum, decubital ulcer of the sacrum, emaciation and an old fibrous scar of the liver. The costal cartilages cut with increased resistance. In the right pleural cavity was about 1 liter of a yellow turbid fluid in the left a slightly smaller amount of a similar fluid. The right lung was irregularly adherent to the parietal pleura as was also the left near the base. The right lung weighed 500 Gm. the left 500. The surfaces of the

2 Delbet, Pierre, and Mendoro. *Epitheliome a cellule independante*. Les Cancers du Sein, Paris, Paris-Masson & Compagnie, 1927 p. 169.

3 In an article now in press. Unusual Bone Carcinoma by Henry B. Thomas. Ed. in H. Primar. Bronchiogenic Carcinoma by Henry B. Thomas. Ed. in H. Primar. and Edwin S. Blaine the interesting conditions found by the authors are described. They were reported by Dr. Blaine in 1927.

Section on Radiology at the meeting of the American Medical Association, Washington, D. C.

right lung were studded with raised, gray masses, from 1 mm to 1 cm in diameter. There were similar masses from 1 to 5 mm in diameter in the pleura of the left lung. The lower lobes of the lungs were not crepitant. Surfaces made by cutting were red-brown, smooth and moist. The peribronchial lymph glands were hard, small and black, with regions of white-gray tissue. The left parietal pleura was red-yellow-brown, studded with firm, raised, white glazed plaques, from 1 to 10 mm in diameter, many of them confluent, the majority linear, parallel to the ribs and averaging 5 mm in width. The right parietal pleura was similar to the left.

The lining of the trachea and main bronchi was very red and covered with a viscid yellow secretion. The tracheobronchial lymph glands were from 5 to 20 mm in diameter, firm and gray-black, and had gray-white regions inside.

On the abdominal surface of the diaphragm was one tumor nodule 5 mm in diameter. Another 10 by 13 mm was in the right lobe of the liver in front under the capsule. The liver weighed 1,820 Gm. A section of the duodenum at the ampulla of Vater was red-brown. The blood vessels were distended, and there were a few subserous gray-white nodules. The mucosa was red-brown, and there were a few submucous hemorrhages. There was no gross change of the heart, thyroid gland, esophagus, stomach, suprarenal glands, kidneys, urinary bladder, gallbladder, prostate gland, spleen, rectum, larynx, testes, epididymides, intestines, brain, pancreas or large blood vessels, except as already mentioned.

A section of the left tibia, 18 by 3.5 by 5 cm, was partially covered by muscle and areolar tissue. The periosteum was firmly adherent, and beneath the periosteum the bone was rough, and on cross-section there was a layer 1 mm thick which was distinctly demarcated from the enclosed cortex. The cortex was hard, the medulla, yellow and soft. The right clavicle was roughened anteriorly 1 cm from the sternoclavicular junction. The periosteum was firmly adherent, but slightly thickened. The underlying bone was smooth, except for the roughened regions mentioned, which were red and extended half the width of the bone. There was a roughened ridge on the anterior and superior surface of the left clavicle, extending 1.5 cm from the distal end of the bone to the middle. There was also a jagged, rough protuberance 1 cm in diameter, 2 cm from the sternocostal junction. The external surface of a piece of bone removed from the anterior crest of the right ilium was smooth and yellow-white. The periosteum was adherent, but not thickened. The cortex was rough hard and yellow-white. The medulla was red. The fifth right rib was smooth, varying from red-brown to gray-brown. The cortex was relatively normal to the amount of cancellous tissue. The cortex was yellow and hard, the medulla was soft and red. The right fourth rib was similar.

After fixation in formalin, the lungs were cut into parallel horizontal segments 1 cm thick and the following was noted. The left bronchus divided abruptly into a large branch to the lower lobe and another to the upper. That to the lower lobe again divided 1 cm from the first bifurcation into two branches, one with a large lumen (8 mm) toward the medial side, the other with a smaller (5 mm) more directly out to the left. The wall of the smaller was 4 mm thick, that of the larger, 2 mm where they arose. Beyond this bifurcation the channels of the branches of the bronchus with the smaller lumen were filled with coagulated mucus, and the thickness of its mucosa 1 cm beyond its origin was 5 mm. The surface of this thick lining was finely granular and warty as compared with that of the other bronchi which had a lining with small parallel longitudinal folds. The tissue of the lung supplied by the constricted bronchus was leathery and contained little air.

*Histology*—In sections through the primary growth in the left main bronchus there were places where the lining epithelium was unchanged. In others it had been mechanically dislodged into the channel. The epithelium in such fragments was unaltered, and the cells had a normal topographic relation to one another. Some such fragments were infiltrated with leukocytes. The tumor was in the tunica propria (fig 5), which was greatly thickened with scattered tumor cells with a leukocytic exudate which varied in amount and with huge lymph channels filled with tumor cells. From this region the tumor had extended into adjacent lymph glands and out through each lung in the lymph channels to the pleura forming there the flat masses noted at the postmortem examination. Extension along lymph channels in the tunica propria and outer coats of the bronchus of the left lung was extensive. Such channels in bronchioles with a lumen diameter

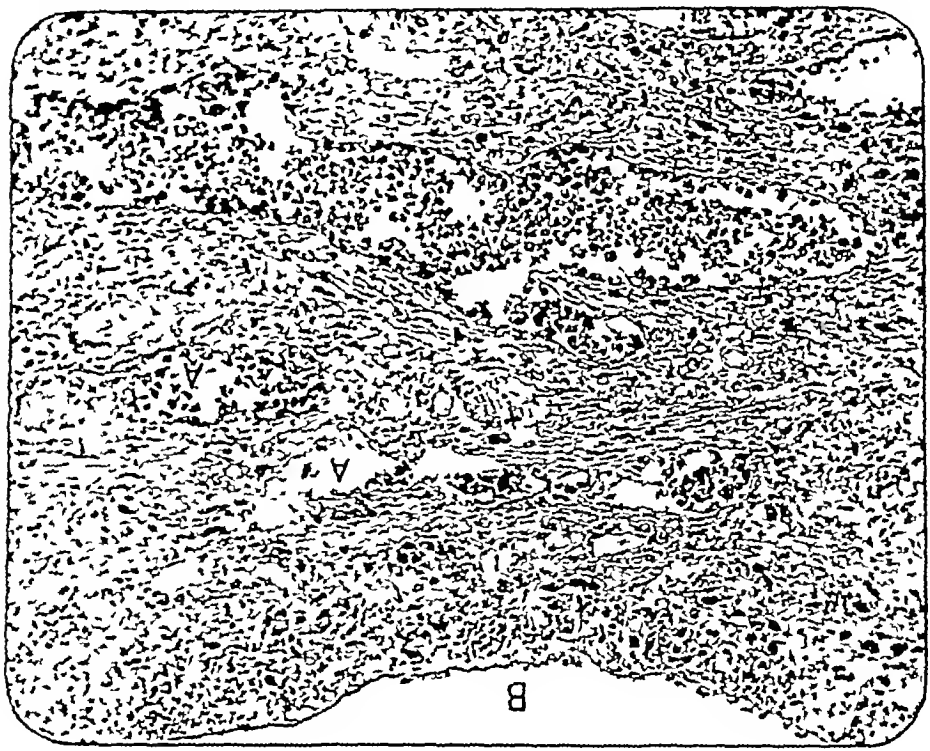


Fig 5—Photomicrograph of the primary carcinoma of the bronchus listed as number 3. The entire surface epithelium is absent. *f* indicates large submucosal lymph channels (veins?) filled with tumor cells. *B* the inner edge of the tunica propria basement membrane for the epithelial lining (absent from postmortem). *A* dislodgement and *C* scattered tumor cells in the tunica propria.

of from 1 to 2 mm were invaded (fig 6) as were the lymph channels. In many places a tissue reaction had resulted in scars or masses of fibroblasts in which all traces of the original lymph channels were lost. In such scars the tumor cells have been lost. Some such scars had developed in the lymph channels of interlobular septums (fig 7) and extended all the way across them. Along their borders were small lymph vessels, circular where cut across and with tumor cells. These regions of thickening were a consequence of the tumor wherever it had developed. The pleural area pathologically

(fig 8) The cicatrization resembled that frequently seen in some mammary carcinomas that grow slowly and deform the regions inhabited by the tumor

The failure to find any tumor in tissue removed at two operations was due, in part at least, to the amount of scar tissue caused by the tumor. This view is supported by the fact that microscopically tumor was absent in tissue from the periosteum and bone where, in a number of places, the outer parts of bones were found rough at the postmortem examination. The number of operations ending with amputation of one forearm, and the difficulty in finding the primary tumor after death are other impressive features of this third bronchiogenic carcinoma.



Fig 6—Photomicrograph of a portion (width 5 mm) of the primary bronchiogenic carcinoma listed as tumor number 3. *A* indicates cartilage, *B*, part of the wall of a pulmonary artery (*C*) with rows of tumor cells in scar tissue similar to figure 4, but in much less magnification, *D*, masses of tumor cells in perivascular lymph channels, *E*, the bronchus and *F*, the normal bronchial glands.

noma. Still another, to be considered later, is the diagnosis of endothelioma made on a number of occasions by pathologists and others at consultations and clinical conferences during the life of the patient.

The fourth bronchiogenic carcinoma was also pronounced an "endothelioma of the bone" by visiting pathologists and surgeons at clinics where the patient and his illness were reviewed. The youth of this fourth patient, a boy, aged 5, the son of a physician, is remarkable



CASE 4—History—The boy was admitted to St Lukes Hospital on June 1, 1925 (to the service of E. W. R.), with pain and lameness of the left leg which began about April 1, 1925, two weeks after an injury of the leg. The pain had been severe, and the periosteum had been incised. One and one-half years before he had a severe attack of influenza followed by an acute otitis media which ruptured spontaneously. After that he had frequent acute infections. The upper and middle third of the left leg was slightly swollen and tender on pressure. There were no abnormal physical signs in the chest or abdomen at this time. The

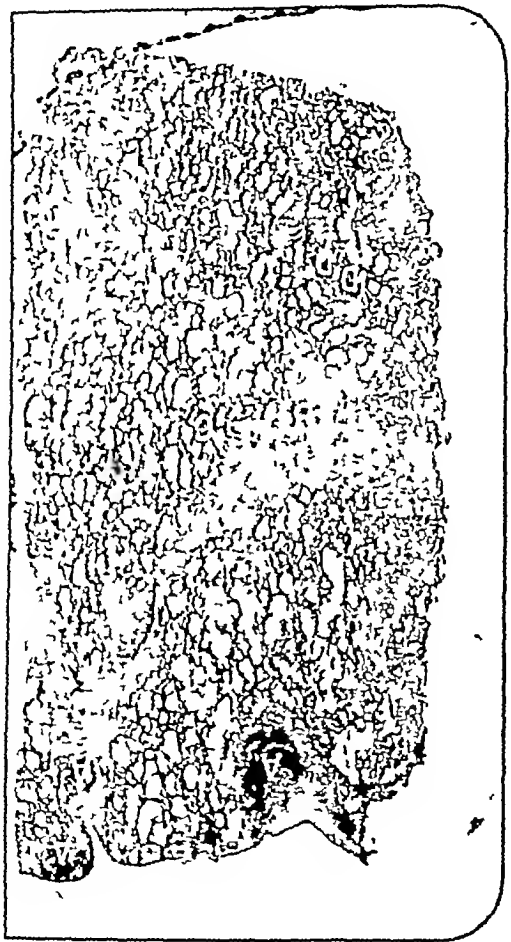


Fig 7—Photomicrograph (tumor number 3) of an entire section 7 b 13 mm, of the lung, X 8. A indicates subpleural lymph channels filled with tumor cells, B, a scarred septum with lymph channel (C) filled with tumor cells, and rows of tumor cells like those in figures 4 and 5 not visible with magnification, and D, the perivascular lymph channel filled with tumor cells.

upper end of the tibia was drained and a little tissue removed. On admission October 14, the upper end of the tibia below the epiphysis was removed. Only necrotic tissue was found by microscopic examination. The upper end of the tibia was drained and a little tissue removed. The proximal end of the removed segment which was 15 cm long. The portion contained eroded bone and soft white tissue some of it necrotic.



*Histology*—The bone was thoroughly replaced by tumor cells in compartments which were generally oblong, the long diameters of which averaged about 0.2 mm, some were twice that length and many were much smaller. The partitions varied from a single capillary with a few fibroblasts to several such vessels, and were thin, delicate and loosely constructed. The cells in these compartments were fairly uniform in size, about as large as the epithelium of the convoluted tubule of the kidney, but with larger nuclei which possessed more chromatin. Generally, there was a narrow empty space between the cells and the stroma of the partitions, an artefact from fixation. The cells were arranged in the smaller compartments much like a tubule with the nuclei at the outer part of the cell toward the stroma and the cytoplasm toward the center (fig 9). The centers of such small groups of cells were therefore paler, the peripheries, dark.



Fig 8—Photomicrograph of a pleural nodule to illustrate the cicatrization so conspicuous in this tumor everywhere (number 3). Compare with figure 4. A indicates the subpleural lymph channels containing tumor cells.

In spite of careful search in these central regions by appropriate staining methods, nothing resembling fibrils (neuroblastoma) was found. The aggregated central cytoplasm of a number of cells was without definite cell margins, it was fairly granular, definitely but slightly basophilic and slightly purple with hematoxylin. The nuclei occupied one half of the cells or a little more and were generally eccentric.

The cells were regarded as epithelium and the growth as a secondary carcinoma.<sup>3a</sup> A careful physical examination following this report failed to locate a visceral tumor.

<sup>3a</sup> Dr. Frank B. Mallory, pathologist at the Boston City Hospital, also concluded this tumor was carcinoma.

In August, 1926, symptoms of involvement of the lung appeared when a fluoroscopic examination was made, for the first time a large shadow was found in the lower lobe of the right lung. A recurrence of the tumor just below the left knee was noted. The patient died on Jan 3, 1927, at Tucson, Arizona, where the postmortem examination was made (E. F. H.)

*Anatomic Diagnosis*—The following diagnosis was made. Huge bronchiogenic carcinoma of the lower lobe of the right lung with extension into the mediastinal lymph glands, metastatic carcinoma of the left lung, the upper lobe of the right lung and thymic body, recurrent secondary tumor of the left tibia, bilateral serofibrous pleuritis, marked distention of the small veins of the esophagus, marked hyperemia of the esophagus, acute catarrhal bronchitis and tracheitis, slight

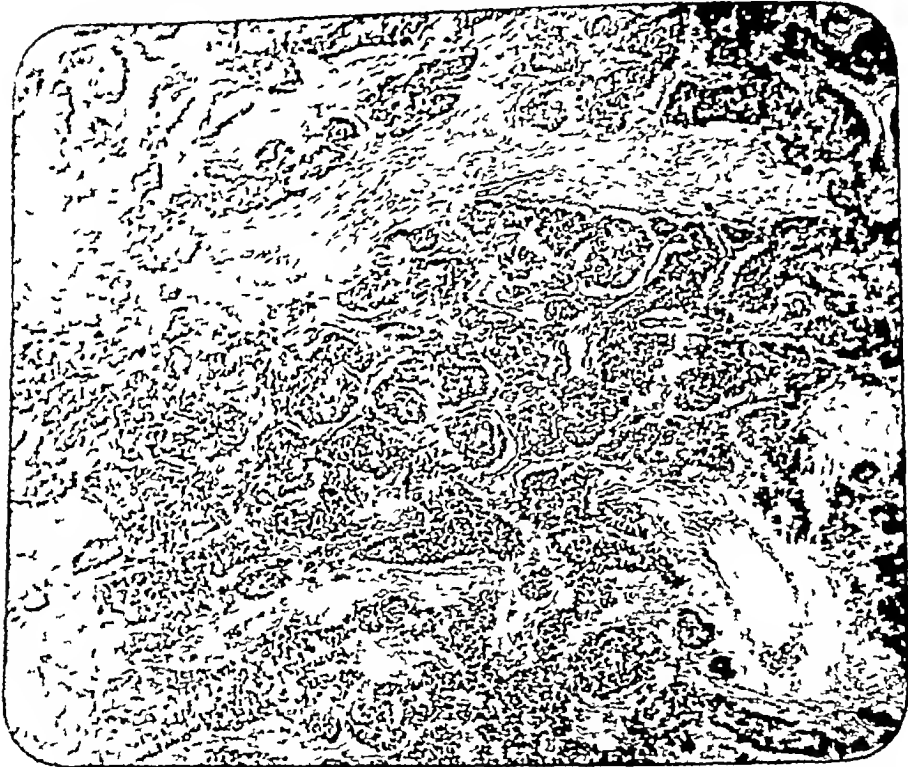


Fig 9—Photomicrograph of tissues in tibia removed surgically. This is a surface of about 4 sq mm. A indicates bone. The pattern of the cells is a feature of these groups (B).

hyperplasia of the biliary, mesenteric and iliac lymph glands and fatty changes of the liver and kidneys. Hyperemia of the edema of the brain and leptomeninges, marked emphysema of the skin of the left leg.

Just below the left patella was a nodular well-circumscribed mass 10 cm, in its other dimensions 8 by 6 cm. This mass was tense and from the upper end a small linear or irregular yellow nodule and had a soft texture. It had grown into the epiphyseal region of the tibia markedly destroying the epiphysis and in the center of the tibia.

cavity for a distance of 2 by 2 cm. There was no bone in the tumor tissue. The right pleural cavity contained from about 200 to 300 cc of a turbid fluid with a few thin flakes of fibrin, the left, about 50 cc. The right lung was firmly adherent to the mediastinum and diaphragm, but not to the wall of the chest. There were no adhesions on the left side between the lung and the wall of the chest. Close to the vertebral column, just above the tenth rib on the right side under the pleura, was a white nodule 5 by 5 by 2 mm. There was a large tumor mass lying in the posterior mediastinum, which was 14 cm long, 8 cm wide and 7 cm thick, and its lower edge was slightly to the left of the midline. It bulged backward so that the aorta arched over the back of the mass nearer the right side than the left. The position of the tumor corresponded to greatly enlarged lymph glands at the bifurcation of the trachea. The trachea was anterior to this mass, and the esophagus at the level of the bifurcation of the trachea was pushed to the left and lay laterally, along the margin of the tumor mass. There was a marked hyperemia of the lining of the esophagus and a marked distention of the vessels of the lining of the lower third, so that they stood out as coarse varicosities. Behind the pericardium and pushing it forward near the midline were two nodular masses, one above the other, the lower 20, the upper about 15 mm in diameter. The lining of the trachea and the left main bronchus to the first branches was pink-gray, unchanged and covered with a thin secretion. The tumor mass in the posterior mediastinum was continuous with another which had replaced most of the lower lobe of the right lung. It was 14 by 12.5 by 6 cm, gray lobulated tissue along the periphery and in the center porous like a fine sponge. The pulmonary vessels were unchanged. The right bronchus leading to the lower lobe passed directly into tumor tissue and could be followed for only about 3 cm. There was a little of the lower lobe along the upper border of this tumor. The lobe was pushed up by the tumor. There was a second tumor 3 by 3 by 2.5 cm in the small amount of remaining lung tissue at the upper edge of the lower lobe, and in the posterior portion of the right upper lobe was a third tumor 7 by 4.5 by 3 cm.

There were two masses of tumor tissue in the left lung, one near the front margin in the upper part of the upper lobe, 2 by 3 by 1.5 cm, the other near the base of the lower lobe, 1.2 by 1 by 1 cm. The lining of the bronchioles of the left lung was unchanged. Surfaces made by cutting these tumors resembled those in the main tumor in the lower lobe of the right lung. The tumor in the left knee had a similar appearance inside. There was no gross change of the heart, suprarenal glands, kidneys, liver, gallbladder, pancreas, stomach, intestines, urinary bladder, prostate, seminal vesicles, testes, epididymides, brain, cervical, iliac, axillary lymph glands or larynx indicative of tumor masses.

After fixation in formalin, the right lung was cut in a coronal plane through the root so as to divide the large tumor in the lower lobe and the other two smaller tumors through their largest diameters (fig 12). From one of the surfaces so made, forty-nine blocks with sizes convenient for sectioning in paraffin were taken by parallel transverse cuts and others longitudinal and at right angles to those across. The blocks, from 5 to 8 mm thick, were given numbers corresponding to those on a diagram the same size and shape as the tissue surfaces, with lines on the diagram matching the incisions of the tissue. In this manner, the location of sections studied was maintained. In a similar way, sections were examined from forty-three blocks from one of the two largest surfaces through the mediastinal tumor which it was possible to obtain with a single bisection.

*Histology*—In only a few of the many sections from the tumors of the lung was there a duplication of the minute structure in the tissue removed at the operation over a year before death. This was only in some of the sections from the lower lobe of the right lung, where the tumor structure was similar in all particulars, small epithelial tubules lying rather loosely in compartments with their nuclei out toward the stroma. In some sections there were masses of tumor cells in small lymph channels about bronchioles, about both pulmonary arteries and veins and in the minute lymph channels just beneath the pleura out and beyond the most peripheral pulmonary acini. In these lymph channels the tumor cells did not have any particular grouping. In the many sections of the large tumor of the mediastinum (thoroughly searched in vain for traces of a teratomaous tumor) and in those from other places in the lungs and recurrent tumor



Fig 10—Photomicrograph of the tissues of the tumor of the lung (no 4). The condition prevailed throughout nearly all of the tumors in the lungs. There is a necrosis (quite regularly spaced) of the tumor cells where in multiplication they grew away from their blood supply. In sarcomas, new blood vessel production along with the tumor cells, as a rule, so that necrosis is infrequent. In the necrotic cells and B, zones of tumor cells separated by vascular fibrous septa.

of the tibia, there was a considerable deviation from that in the tibia examined. The original arrangement of single layers of epithelium (fig 9) was replaced by one with from fifteen to twenty cells in layers. The cells also in compartments and in many of these the cells had a high degree of differentiation from their blood supply had undergone necrosis. In many of the sections one dimension was much greater than the others.

stalklike formation<sup>4</sup> occurred in many sections, stalks of vessel-bearing stroma on which the epithelium rested, and all about between such branching bands there was necrotic epithelium in varying amounts. This type of growth is common in the papillary tumors of the urinary bladder, renal pelvis and proliferating papillary cystic tumors of the ovary, especially those with considerable masses of tumor. Its best examples are met with in the secondary metastatic and recurrent growths of such tumors.

Because of the youth of the patient and the extreme rarity of a primary bronchiogenic carcinoma at his age, every effort was made to discover some evidence against the conclusion that the tumor originated in the lung tissues. Bone



Fig 11—Photograph of the tumor growth projecting into the lumen of the left bronchus (tumor number 2)

metastases have been reported<sup>5</sup> with neuroblastomas, but careful search has failed so far to demonstrate that the lung, mediastinal and bone tumors of this boy are of this nature. The contention may be made that the bone tumor was the primary growth, and that the lung and mediastinal tumors were secondary. The arguments against this and in favor of the conclusion that the primary tumor was in the lungs are (1) the gross appearance of the tumor in the lungs (fig 12), its close relation with and distribution around a large branch of the bronchus,

4 LeCount, E. R. The Genesis of Carcinoma of the Fallopian Tube in Hyperplastic Salpingitis, Report of a Case and a Table of Twenty-One reported Cases, *Bull. Johns Hopkins Hosp.* **12**: 55, 1901.

5 Wahl, H. R. Neuroblastoma, *J. Med. Research* **30**: 205, 1914.



## REVIEW OF THE LITERATURE

There are many<sup>7</sup> reports mentioning the increased frequency of carcinoma of the lungs, not a few ascribing a causal relation to the pandemic of influenza. The basis for this conclusion follows from studies<sup>8</sup> of the lungs in influenza which describe a hyperplasia of the bronchial epithelium or a metaplasia of the lining cells into pavement epithelium, like a precancerous growth. Meyer<sup>9</sup> has reported a bronchiogenic carcinoma, which he thinks was originated by an attack of influenza.

Of the 74 primary carcinomas of the lung reviewed by Passler,<sup>10</sup> secondary tumors were found in the bones with 12, Adler<sup>11</sup> mentions 57 with 374 primary carcinomas of the lung and the bronchus, Grove

7 Among these reports are

Payr, E. Extirpation eines grossen, primären Plattenepithelkrebses der Lunge, *Arch f klin Chir* **133** 700, 1924

Mathias, E., in Discussion on Teutschlaender, O., and Stahr, H. *Verhandl d deutsch path Gesellsch* **19** 190, 1923

Berblinger, W., in Discussion on Teutschlaender, O., and Stahr, H. *Verhandl d deutsch path Gesellsch* **19** 190, 1923, Die Zunahme des primären Lungenkrebses in den Jahren 1920-1924, *Klin Wchnschr* **4** 913, 1925

Verse, M., in Discussion on Teutschlaender, O., and Stahr, H. *Verhandl d deutsch path Gesellsch* **19** 191, 1923

Bejach, H. E. Beiträge zur Statistik des Carcinoms, *Ztschr f Krebsforsch*, **16** 159, 1919

8 These studies are found in the following articles

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Schmidtmann, Martha. Einige bemerkenswerte Beobachtungen zur Pathologie der Grippe, *Virchows Arch f path Anat* **228** 44, 1920

Mittasch, G. Ueber die pathologisch-anatomischen Grundlagen der Influenza mit besonderer Berücksichtigung der Gehirnveränderungen, *Frankfurt Ztschr f Path* **26** 406, 1922

Winternitz, M. C., Wason, I. M., and McNamara, F. P. *The Pathology of Influenza*, New Haven, Yale University Press, 1920, p 48

Gaus, A., and Fritzsche, R. Ueber den Sektionsbefund bei der gegenwärtigen Grippe-Epidemie unter besonderer Berücksichtigung der mikroskopischen Befundes *Cor Bl f schweiz Aerzte* **49** 72, 1919

9 Meyer, B. Ein Fall von Epithelmetaplasia und metaplasierendem Carcinom des rechten Hauptbronchus nach Grippe, *Frankfurt Ztschr f Path* **27**. 517, 1922

10 Passler, H. Ueber das primäre Carcinom der Lunge, *Virchows Arch f path Anat* **145** 191, 1896

11 Adler, I. *Primary Malignant Growths of the Lungs and Bronchi*, New York, Longmans, Green & Company, 1921

and Kramer,<sup>12</sup> 8 among 21, and Seyfarth,<sup>13</sup> in a report of 307 carcinomas of the lung, said that metastases in bones occur often chiefly in the ribs, sternum and vertebrae, but rarely in other parts of the skeletal system. It is known, however, that in routine postmortem examinations these bones usually are examined, and many others are not. Commenting on the studies of carcinoma in general by C. Frankel and Fischer-Defoy in which from 26 to 28 per cent of bodies had metastases in the skeleton, Schmorl<sup>14</sup> stated that these figures are too low because only those recognized grossly are reported, whereas a microscopic examination of the bones increases the figures by 6 per cent. He also found secondary growths in bones in bodies with no tumors of viscera usually invaded secondarily.

Dosquet<sup>15</sup> failed to state the number of secondary tumors of the bone in the 105 primary carcinomas of the lung that he found recorded in 2,519 postmortem examinations. All were made by Lubarsch or his assistants, 2,158 at Berlin and 361 at Kiel. Dosquet's review is limited strictly to the frequency of secondary carcinomas in the central nervous system and in the suprarenal glands. He found that secondary tumors developed in these two regions from carcinomas of the lung and from bronchial carcinoma with much greater frequency (from 21.8 to 31.4 per cent) than from other carcinomas (from 0.6 to 3.9 per cent). He also stated that Orth, Vögeler, and Goldmann found regularly in invasion of the veins, a so-called "endophlebitis carcinomatosa" with both primary and secondary carcinoma of the lungs which may account for the widespread metastases in the viscera. Schmorl thought that bone marrow favors the growth of metastatic carcinoma tissue.

When histologic examinations are made of the metastatic tumors from primary carcinomas of the lungs, the reports regularly state that the cellular structure is like the primary growth. This, of course, is to be expected, and the structure may be that of "identical carcinomas" (cylindric cells), in which there are glandlike structures lined by one or several layers of cylindric epithelium or large papillary stalks suggesting a papillary adenocarcinoma; the cells sometimes contain vacuoles with mucin or arranged in alveoli filled with a muciniferous substance. (2) carcinoma samples in which irregular solid nests of

12 Grove, I. S. and Kramer, S. L. Primary Carcinomas of the Lung.

M. Sc. 171, 250, 1926.

13 Seyfarth, C. Lungentumoren in Leipzig. Deut. Arch. f. klin. Med. 50, 1497, 1924.

14 Schmorl, L. Über Krebsmetastasen in Knochen. Z. f. Krebsforsch. 12, 80, 1908.

15 Dosquet, L. Über die Metastasenbildung. Z. f. Krebsforsch. 12, 80, 1908.

16 Barron, M. Carcinoma of the Lung. J. Clin. Path. 1, 2, 1948.



cords of undifferentiated epithelial cells are surrounded by a connective tissue stroma, (3) alveolar carcinoma, in which there are large solid masses of pleomorphic cells occupying spaces resembling lung alveoli (4) medullary carcinoma in which the cells are small, compact and pleomorphic and have little cytoplasm, this form is sometimes distinguished from sarcoma with difficulty, (5) colloid carcinoma

Primary tumors of the lung giving rise to the metastases vary much in size and appearance. The large bulky tumors are easily recognized, the small ones, sometimes with difficulty. It is generally conceded (Passler, Kikuth, and others) that practically all are bronchiogenic tumors. According to Passler, many are anatomically nearly pure bronchial tumors. Either the bulk of the carcinoma is in the bronchial lumen, constricting and even occluding it, or the tumor develops in the loose peribronchial tissues and penetrates deeply into the substance of the lung. This peribronchial tissue, especially, is involved by the carcinoma, the parenchymatous tissues for large regions are unchanged or show only secondary changes, such as inflammation and compression. Kikuth,<sup>17</sup> in writing about the material at the Eppendorf Hospital, said that these tumors vary greatly in size. They usually lie within a few centimeters of the bifurcation of the trachea, near the origin of the bronchi leading to the individual lobes. There may be an irregular rough thickening of the bronchial mucosa or extremely small and scarcely elevated regions occupying only 3 sq mm of surface. Sometimes the lymph channels are extensively invaded by carcinoma, so that the whole lung, one lobe especially, is studded with innumerable submillary masses that fill the lymph and blood vessels along the bronchi, extend to the pleura and there form pearly aggregates.

It is scarcely necessary to say that many of these metastases to the pleura have been reported as "endotheliomas," because the postmortem examination and histologic studies failed to reveal the primary tumor. Robertson's<sup>18</sup> extensive analysis of "endothelioma" of the pleura closes with the following statement:

This review apparently proves that only the sarcomas can be classified as primary malignant tumors of the pleural tissues, and that all other growths are secondary, representing extensions, implantations, or metastases from an unrecognized or latent primary source (carcinoma), usually the lungs.

These conclusions by Robertson as regards the "endotheliomas" of the pleura raise a similar doubt as regards the "endotheliomas" of bones.

<sup>17</sup> Kikuth, W. Ueber Lungencarcinom, *Virchows Arch f path Anat* **255** 107, 1925.

<sup>18</sup> Robertson, H. E. "Endothelioma" of the Pleura, *J Cancer Research* **8** 316, 1924.

An analysis of the reports<sup>1</sup> designated as endothelioma or homoblastoma prior to 1919 demonstrates that only those by Engelmann, Jaffe, Sudhoff, von Lukowicz, Zahn, Spiegelberg, Volkmann, and Howard and Crile contain details of postmortem examinations. Engelmann described a huge tumor of the right side of the chest appar-

19 These reports are given in the following articles

Lueke, A. Beiträge zur Geschwulstlehre Virchows Arch f path Anat 35 524, 1866

Kocher, T. Zur Kenntnis der pulsierenden Knochengeschwulste nebst Bemerkungen ueber hyaline Degeneration (resp. Cylindroma), Virchows Arch f path Anat 44 311, 1868

Billroth. Ueber alveoläre Sarcome, Arch f klin Chir 11 244, 1869

Engelmann, G. J. Ueber einen alveolären Tumor mit collöder Degeneration, Inaug Diss, Berlin, 1871

Jaffe. Zur Kenntnis der gefäßreichen Sarcome, Arch f klin Chir (Langenbeck) 17 91, 1874

Sudhoff, K. Ueber das primäre multiple Carcinoma des Knochen-systems Inaug Diss Erlangen 1875

Schwemmer, L. Kurze Mitteilungen aus den pathologischen Anatomischen Demonstrationen des Prof Dr v Buhl in München. Vierteljahrsschrift f Anat 23 339, 1876

Von Lukowicz, J. Ein Fall von Gallertgeschwulst des Os femoris. Inaug Diss, Halle, 1879

Kolaczek. Acht neue Fälle von Angio Sarcoma. Deutsche Zeitschr f Chir 13 1, 1880

Zahn, T. W. Leber Geschwulstmetastase durch Capillarsarcoma, Virchows Arch f path Anat 117 1 1889. Beiträge zur Geschwulstlehre, Deutsche Zeitschr f Chir 22 14 1885

Hildebrand. Ueber das tubuläre Angiosarcoma oder Endotheliom d. Knochen. Deutsche Zeitschr f Chir 31 263 1891

Driesen, L. F. Untersuchungen ueber physiochemische Endothelien. Ziegler's Beitr 12 65 1893

Spiegelberg, H. Beiträge zur Kenntnis der multipel auftretenden Knochen-sarcome Inaug Diss Frankfurt 1894

Volkmann, R. Leber endotheliale Geschwulste. Inaug Diss, Leipzig, 1895

Markwald. Leber sogenannte multiple Alveolare Geschwulst. Virchows Arch f path Anat 5 850 1894. Ein Fall von multipel auftretendem Endotheliom in den gesammten Knochen des Skelets. Virchows Arch f path Anat 141 128 1895

Graward, L. De l'Endotheliome des Os. Thèse Paris 1895

Ritter, C. Der Fettgehalt in den Endothelzellen. Virchows Arch f path Anat 141 128 1895

Berger, P. Sur les endotheliomes des os. Revue de Chir 50 247 1895

Sternberg, C. Ein Fall von multipel auftretendem Endotheliom. Virchows Arch f path Anat 141 128 1895

Anat 12 625 1904

ently arising from the ribs, which histologically resembled a colloid struma. The compressed right lung contained small metastatic tumors, but the bronchial and other lymph glands were unchanged. These statements include all the details of the postmortem examination. Jaffé mentioned a tumor of the left ilium and small gray nodules in the lungs and pleura. These contained cells arranged in acini and cylindrical rows. The account of the postmortem examination is brief and a careful examination of the lungs for a primary tumor is not mentioned. The details of the postmortem examination by Sudhoff are meager. He described, in tumors of many bones, tissue like a "glandular carcinoma." Von Lukovicz reported a colloid tumor of the right femur and pelvis found postmortem in the body of a man, aged 60. In the left pleural cavity were more than 25 liters of a bloodstained fluid. The lung was compressed, and the pleura was thickened by (small ?) smooth, flat, tumor masses. The tumor of the femur was composed of tubular structures, some of the lining cells were cylindric. No mention is made of an examination of either lung for a primary tumor. This account is preceded by reference to two reports of metastases of the bone with primary carcinoma of the thyroid. In a discussion of his own observations, von Lukovicz considered the possibility that the tumors are metastases, he was uncertain that the tumor of the bone was primary. The tumors of the bone and pleura, he said, are alike, histologically. He did not make a microscopic examination of the thyroid gland. The tumor at the base of the skull described by Zahn contained alveolar and tubular structures. He regarded the tumor as primary in the skull, but failed to consider the epithelial structures present in these regions.

The dissertation by Spiegelberg contained only a few details of the postmortem examination of a woman, aged 62, who had tumors of the

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Howard, W. T., and Crile, G. W. A Contribution to the Knowledge of Endothelioma and Perithelioma of Bone, *Ann Surg* **42** 358, 1905

Symmers, D., and Vance, M. Multiple Primary Intravascular Hemangio-endotheliomata of the Osseous System Associated with the Symptoms of Multiple Myelomata, a Lesion Hitherto Undescribed, *Am J M Sc* **152** 28, 1916

Ewing, J. Diffuse Endothelioma of Bone, *Proc New York, Path Soc* **21** 17, 1921, *Neoplastic Diseases*, Philadelphia, W. B. Saunders Company, 1919, pp. 312-314, A Review and Classification of Bone Sarcomas, *Arch Surg* **4** 485 (May) 1922

Kolodny, A. A Case of Primary Multiple Endothelioma of Bone with Special Emphasis on Its Roentgenologic Features, *Arch Surg* **9** 636 (Nov.) 1924, *Bone Sarcoma*, *Surg Gynec Obst* **44** 126, 1927

Coley, W. B., and Coley, B. L. Primary Malignant Tumors of the Long Bones, *Arch Surg* **13** 779 (Dec.) 1926, *ibid* **14** 63 (Jan.) 1927

ribs, sternum, right ilium and spleen. The right pleural cavity contained a quantity of turbid fluid, and the lung was markedly compressed. The tumors of the bone contained nests of cells about the size of medium large pavement epithelium, some arranged in tubules and in cylindrical structures. These, Spiegelberg said at first suggested a metastatic tumor, and he mentioned search in the mammae (spleen-pancreas and intestinal tract for a primary growth but he said nothing about an examination of the lungs, bronchi, thyroid or certain other viscera for primary carcinoma. He also included a report of a frontal and a sacral tumor received from Ziegler. Histologically these had alveolar structures and resembled those first mentioned. There is no mention of a postmortem examination. Volkman in his introductory paragraph on "Endotheliale Knochengeschwulste," stated that all of these tumors contain tubules and alveolar structures of epithelial-like cells, often cylindrical, which undergo mucoid or hyaline degeneration or secrete mucin and hyaline substances. Writing at that time (1895) he said that if the morphologic characters of the cells are considered without regard to their genesis, these tumors can be accepted as evidence of a "primary bone carcinoma". He described a huge tumor of the skull in a man, aged 70, who died ten days after the miss had been excised. Postmortem examination did not reveal any metastases in the body. In the details of this autopsy record edema and emphysema of the lung are mentioned. Microscopically, the spindle cell stroma of the tumor contained ductlike structures with cylindric epithelium that resembled closely, as he said a carcinoma of the bowel. Volkman also included a description of tissues given him by Dr. Marth and these being the ones von Lukowicz described in his dissertation. Volkman thought that the pleural tumors unquestionably are endothelial but von Lukowicz said that the cells in these growths cannot be distinguished from epithelium.

The report by Markwald, in 1895 is mentioned frequently in connection with the cardinal features of these so-called endotheliomas of the It records the results of a postmortem examination of the body of a man aged 56 which demonstrated destructive tumors of the bones (calvarium vertebrae ribs bones of the pelvis and scapulae, etc.), but none in the viscera. The tumors consisted of arranged in solid masses and cords which he says, were composed of brief statements of the postmortem examination the left carcinoma. A vascular fibrous stroma supported these cords. The brief statements of the postmortem examination the left had sharply circumscribed solid pieces that contained a hypostatic pneumonia in the lower and middle lobes. The report of a histologic examination of the lungs

a careful examination of the bronchi for carcinoma. Markwald seems to have been uncertain in his interpretation of these tumors because the title of his brief account is "Ueber die sogenannte multiple myeloma", that of his more extended report includes the terms "myelom, angio-sarcom". It is clear, at least, that in assuming a multiplicity of primary tumors of bones he is incorporating ideas generally held regarding multiple myelomas, and so he does not differentiate between a primary tumor and tumor metastases.

The tumors of the bones in the body of a woman, aged 66, described by Sternberg were limited to the medulla and did not destroy the cortex. The cells in these tumors were "signet ring" like those of a Kruckenberg tumor of the ovary, and are unlike those in other descriptions of these tumors of the bone. One of the two autopsy reports by Howard and Crile mentioned changes like those contained in the reports by Jaffé and von Lukovicz, the other described such widespread tumor growths that even the authors were in doubt as regards the primary tumor. This, they thought, was somewhere in bones, although grossly the tumor tissues resembled carcinoma.

Other reports (Lucke, Billroth, Schweiniger, Spiegelberg [case 2], Kolaczek, Hildebrand, Driessen, Gaynard, Ritter, Berger, Howard and Crile [case 2], Simmers and Vance) sometimes mentioned with this group of tumors, are without the results of postmortem examinations and are based on the study of surgical material. These reports, in general, make little comment about the further progress of the disease, and the conclusions permitted by a study of such material are limited.

After these earlier reports there was little mention of "endotheliomas" of the bone until the accounts by Ewing. These described three varieties: (1) the multiple endotheliomas, which involve many bones, occur usually in adults, generally are fatal with metastases to the lungs, and are composed of endothelial-like cells in small groups or "sheets," often alveoli, and sometimes contain cysts with serous or mucinous fluid, (2) angio-endothelioma, and (3) solitary diffuse endotheliomas which occur in young patients.

The single bulky circumscribed tumors arise in the bone marrow, soon perforate the cortex and develop externally. The structure is a tubular or alveolar endothelium, mucoid and hyaline degeneration occurs, and cysts may be present. Typical of these tumors are the two described by Volkmann. But, as has been mentioned, Volkmann stated that the one of the skull closely resembles a carcinoma of the bowel, while the other of the right femur, described originally by von Lukovicz, occurred in the body of a man with multiple small tumors of the left pleura, like metastases of a primary lung or other carcinoma. The multiple endotheliomas of the bone affect nearly every bone in the body, as described in the report by Markwald.

There is no mention of the results of careful postmortem examinations in any of these accounts by Lwing and in the discussion of his report at the meeting of the New York Pathological Society. Dr Symmers asked whether there was any possibility that these patients suffered from a primary tumor of the kidney notably the so-called hypernephroma which often metastasizes to bones and the structure of which is not unlike that of the preparation illustrated

Kolodny reported "a primary multiple endothelioma of bone, based on the study of surgically removed tissues and of tissues obtained by a postmortem examination. The first statements of the microscopic examination are as follows: "The arrangement of the tumor cells in alveoli and tubules was similar to that of an adenomatous growth. This together with the large-sized cylindrical and polygonal flat cells abundantly present in the sections, easily gave an impression of a carcinoma. His subsequent statements argue in favor of origin from blood vessel endothelium. The mediastinal and mesenteric lymph nodes were involved extensively, and the lungs contained multiple primary nodules. It is regretted that the report contains so little of the details of the postmortem examination (by Dr Orton). The only statement being on the thoroughness is contained in the sentence: "The necropsy was performed as completely and carefully as possible. Dr Orton giving especial attention to the possible occurrence of a primary tumor of the soft tissue." There is no discussion of the significance of multiple tumors in the lungs and lymph nodes.

A summary of fifty-four endotheliomas of bones in the collection of the American College of Surgeons is contained in a report by Connor. Approximately one half of the fifty-four patients mentioned by Connor died according to his statements postmortem examination was made in less than one third. Careful study of his individual reports available to us of course may not contain all of the information available to us to demonstrate just how completely or thoroughly any of these postmortem examinations were made. There also is considerable doubt as to the final status of the patients based on living. Connor did not give an example in a somewhat later report and that one of the patients reported in Connor's list as living is dead possibly as a result of metastasis but add that no postmortem examination was made. The patient lived at least five years after the operation. Only six others in the entire list on living are reported that have lived as long or longer. Only twenty-six patients with tumors were observed of the bones. Accounts of postmortem examinations of those dead are not contained in the report. Of these diagnoses were made as follows:

histologic examination of the tumor Kolodny's report of the material contained in the registry of bone sarcomas of the American College of Surgeons has a section dealing with these tumors designated as "Ewing's sarcoma" His account is a restatement of features already mentioned and includes no new information gained by postmortem examinations

Of the reports after 1919, the ones by Ewing do not contain any statements of the results of postmortem examinations, and the one by Connor mentions such results only in a general way Of the 18 patients that died (cases 30, 31, 33, 36, 37, 38, 39, 40, 41, 45, 46, 47, 48, 50, 51, 52, 53, 54) and in which some mention is made of tumors other than the ones first recognized clinically in bones, there are thirteen which specifically record the presence of tumors of the lungs Of the eighteen patients reported by Coley and Coley (Cases 4, 8, 9, 11, 20, 21, 22, 23, 25, 32, 34, 36, 37, 42, 43, 48, 49 and 54), five died, and the body of only one was examined post mortem Accounts of this examination (case 49) are limited to the brief comment that there were "very extensive metastases into nearly every organ and bone of the body"

These solitary and multiple destructive tumors of bones containing masses of cells resembling epithelial structures, such as alveoli and tubules, have been designated primary endotheliomas because the cells are said to be arranged along the walls of capillaries and because of certain details of internal structure The use of this term implying origin from vascular tissue seems to have begun at a time when Virchow's teaching that carcinoma may arise from connective tissue was discarded, and in explanation of the presence in bones of tumors resembling carcinoma some vascular tissue derivation was offered In not a few instances this deduction has followed directly, and the author has been in considerable ignorance of the conditions in other parts of the body of his patient at the time his report was written, because he had only surgical material for study In other instances, when tissues obtained by postmortem examination were studied, conclusions of vascular origin were drawn because a primary tumor was not found in the viscera Among these are reports in which doubt exists as regards the thoroughness and completeness of the examination That solitary vascular tumors occur is not denied, and that secondary growths (metastases) originate from a primary malignant tumor also follows in logical order In none of the reports mentioned, however, except the one by Connor, is the mechanism of metastasis from a primary tumor considered in explaining the presence of the so-called multiple primary endothelioma in many bones Instead, each tumor is regarded as arising independently

A number of years ago, Bassoe<sup>20</sup> reported a primary tumor of the pleura with the outstanding feature that the growth produced an unbroken chain of proliferating lymph channels which extended from the cervical and axillary glands above, along the right pleura through the lymphatics of the diaphragm, and spread over the entire parietal and visceral peritoneum to the thoracic and pelvic lymph nodes below. Isolated metastases were not found in any organ. Bortmann<sup>21</sup> in a critical review years ago, took the stand that many reports of endothelioma really concerned carcinoma. He emphasized the tendency to describe as endothelioma any tumor with cells arranged in cords and agreed with Bender that no dependence should be placed on the relation of tumor cells to the lining cells of the lymph channels as a criterion of endothelioma.

The assumption of multiple primary foci in bones as an explanation of coincident tumors in various parts of the skeleton seems due to the failure to find a small primary carcinoma in the relatively small number of postmortem examinations of the bodies of these patients or to the inability to distinguish the primary growth from the secondary in the presence of many tumors in different tissues. Therefore, it is generally held in explanation of the existence of multiple myelomas in bones that been included with the "multiple endotheliomas of bones." As the result of such interpretations of a limited postmortem material there are many reports based only on the examination of tissues removed surgically without regard for conditions in other parts of the body. Some of these have been made at a time when the ultimate clinical result in the patient could not be determined was unknown, or perhaps not sought.

This dearth of information about conditions elsewhere than in the bones in the bodies of these patients is probably the greatest obstacle to the way of gaining a generally accepted opinion of the position of the so-called "endotheliomas" among the tumors of bones. Such information will be obtained by careful and thorough post-mortem examination of the bodies of these patients supplemented by a thorough necropsy of the changes thereby demonstrated. Most of the difficulties in the diagnosis of these tumors mention the care necessary to avoid against a confusion with metastatic carcinomas. It would be unfortunate, therefore, that conclusions drawn from studies based on the removal of removed tissues without a careful post-mortem examination of the body through physical and roentgen-ray examination.

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## SUMMARY

Metastases to bones, as stated by others, occur in a large number of patients with primary carcinoma of the lungs

In a certain number of patients with such secondary carcinomas, the symptoms caused by the tumors in the bones dominate the clinical course of the disease

The clinical course and the results of postmortem examinations are reported in four patients in whom the bone metastases from a primary carcinoma of the lungs caused the chief symptoms

The secondary tumors removed surgically from two of the patients during life were diagnosed by some pathologists as so-called "primary endothelioma" of the bone

One of these primary carcinomas of the lungs with metastasis to the left tibia occurred in a boy 6 years of age at the time of death. A year before he died, tissues of the tumor of the bone were diagnosed metastatic carcinoma, and at that time a careful physical examination failed to disclose the primary tumor

An analysis of the reports of so-called endotheliomas of bones demonstrates that many of these are based on a study of tissues removed surgically from patients whose bodies were not examined after death, or were examined without the care necessary to disclose a primary carcinoma, especially of the lungs

Metastatic carcinomas are easily confused with other tumors of the bones, and therefore a diagnosis of "endothelioma of bones" in surgically removed tissues containing epithelial-like cells in alveoli and tubules, has doubtful basis. A thorough and careful postmortem examination later, by which all parts of the body are examined, provides the necessary information for a correct conclusion. The results of the postmortem examinations reported here demonstrate that tumors said by some to be endotheliomas of bones occurred in bodies in which we believe there is a primary carcinoma of the lungs

In the search for a primary tumor in patients with carcinoma metastases in bones, the lungs should be included among the probable sources

# SINUS PERICRANII (REDUCIBLE BLOOD TUMOR OF THE CRANIUM)

ITS ORIGIN AND ITS RELATION TO HEMANGIOMA AND ABNORMAL  
ARTERIOVENOUS COMMUNICATION REPORT OF A CASE

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Sinus pericranii is the name most frequently used in the European literature to designate a blood cyst or hemangioma of the pericranium communicating with an intracranial blood sinus by one or more abnormal foramina in the skull

Clinically, sinus pericranii presents a soft, compressible, fluctuant swelling which increases in size when the patient assumes a posture with the head down, when he flexes his neck sharply, or when he raises his intrathoracic pressure by coughing, crying or making an expiratory effort with the glottis closed. Digital compression of the jugular veins also causes the swelling to grow larger. Indeed, the lesion may not be apparent unless some of the factors that increase intracranial venous pressure are active. A bluish color is sometimes visible through the skin over the swelling, but when it is not, the tumor is easily mistaken by the unwary for a meningocele. The roentgenogram of the skull generally shows an area of rarefaction or a perforation corresponding to the situation of the tumor

Few, if any, symptoms accompany the anomaly. Pain of moderate severity and vague cerebral disturbances have been recorded in some of the reported cases. The age incidence is from birth to late maturity. Many of the cases in older subjects are significantly related to antecedent trauma. In most of the cases, the lesion has been progressive, frequently starting as a small nodule and gradually developing into a tumor several centimeters in diameter.

When first described and named by Stromeyer, and for many years thereafter, the lesion was considered a *noli me tangere*. When treatment was administered, the methods were generally such as to destroy the specimen as far as any pathologic investigation was concerned. In more recent years, aggressive surgical methods of treatment have yielded specimens for examination. Nevertheless, it is remarkable that few searching pathologic examinations are recorded. From most of the descriptions, which are sufficiently detailed to warrant judgment, it

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\* From the Laboratory of Surgical Pathology of the Indiana University School of Medicine. The permission of Dr. W. D. Gatch to publish the case reported in this article is hereby acknowledged.

appears that the lesion is generally of the nature of a cavernous hemangioma. It is usually circumscribed and limited to the pericranium. One or more anomalous emissary veins, piercing foramina in the skull, place the blood spaces of the tumor in relation with one of the large intracranial blood sinuses. In the recorded cases available there has been a singular paucity of careful notes regarding tributary vascular channels in the pericranium.

The lesion must be relatively unusual. Mastin,<sup>1</sup> in 1886, found fifty-five references in the literature. Only three of these articles were in the English language. Cohn,<sup>2</sup> in 1926, found fourteen additional references, one of which was in English, but overlooked the excellent paper by Mastin, who reported the first American case so far as can be determined. Cohn cited Cushing's<sup>3</sup> brief reference to the condition in Keen's "Surgery." I have collected sixteen additional references, three of which are in the English language. I was able to find eighty-four references to articles on this condition, seven of which are in English, including Cushing's brief description.

It is improbable that the disparity between the literature in English and in foreign languages is due to the fact that a greater number of cases have occurred in continental Europe. It is altogether more likely that the cases reported in England and America are lost in the literature under such titles as "angioma," "aneurysm by anastomosis," and "cirroid aneurysm." Mastin listed fifteen terms under which he found the condition described. These are thought worthy of quotation, together with four others which I have added: *Varix verus cirsoideus*, *varix verus circumscriptus*, *fistule osteo-vasculaire*, *erectile tumors of the skull communicating with the superior longitudinal sinus*, *sinus pericranii*, *varix sinus verus extra-cranium congenitalis*, "venous tumors" of the cranial bones, *varix spurius circumscriptus venae diploicae frontalis*, *sanguineous hernias of the vault of the skull by communication with the intracranial venous circulation*, *sanguineous hernias of the vault of the skull by communication through openings in the bone of the meningeal vessels with the exterior integument*, *varicose veins or venous varicosities of the skull*, *a new form of tumor of the vault of the cranium, produced by the blood in communication with the intracranial venous circulation*, *subpericranial venous tumors*, *reducible sanguineous tumors of the vault of the cranium*, *aneurysmal tumors of the temporal region*, *cephalematocoele*, *hemangioma*, and *cavernoma*.

1 Mastin, W. M. Venous Blood Tumors of the Cranium, *J. A. M. A.* 7 309 (Sept. 18) 1886.

2 Cohn, Isidore. Sinus Pericranii (Stromeyer), *Surg. Gynec. & Obst.* 42 614, 1926.

3 Cushing, Harvey. Sinus Pericranii, in Keen, *Surgery*, Philadelphia, W. B. Saunders Company, 1919, vol. 3, p. 33.

I believe that the name sinus pericranii should be applied consistently to the lesion in question in consideration of the peculiarities that it owes to its special relation with intracranial circulation, regardless of the pathologic category to which it may eventually be assigned. This name has the additional merit of priority and historical association.

#### REPORT OF A CASE

The patient with the case of sinus pericranii to be described in the following paragraphs was referred by Dr B R Kirklin, now of the Mayo Clinic, to Dr W D Gatch who performed the operation, at which I assisted.

A T, aged 16, was admitted to the Robert W Long Hospital, March 28, 1923, complaining of pain in the forehead associated with a tumor under the skin in that region. The family history did not present any significant facts. The patient fell on a stone at the age of 5 years, cutting his forehead at the site now occupied by the tumor. The wound healed uneventfully. At the age of 8, a small, hard lump appeared on the right side of the forehead just below the hair line. The lump was painful, and the skin over it was tense. The lump later became soft and gradually increased in size. The patient occasionally had headache associated with throbbing pain in the affected area, otherwise there were no neurologic symptoms.

The patient was of good physique and well nourished. There were no abnormalities other than the tumor. It was not present when the patient stood or sat erect. On close inspection, an area of skin 4 cm in diameter at the right of the midline just below the hair line appeared a little coarse in texture. Palpation of this area revealed an oval depression about 3 mm deep in the cranium. The bony border was irregular but not appreciably raised. The floor of the depression was flat, and no orifice could be felt in it. When the patient inclined the head forward, a rounded tumor gradually appeared. The color of the skin did not change. Palpation now revealed a soft, fluctuant mass which did not move over the cranium, but over which the skin was freely movable. There was no pulsation, thrill or bruit. The mass was opaque to transillumination. The roentgenogram made by Dr Kirklin showed an area of apparent complicate absence of bone in the region occupied by the tumor. At the margin of this defect, the tables showed an angular separation. A visiting surgeon, by no means inexperienced, considered the lesion a meningocoele. Nevertheless, the preoperative diagnosis was "hemangioma communicating with the intracranial circulation."

Under ether anesthesia, a U-shaped incision was made. The limbs extended upward, outlining a flap exceeding the tumor in size by about 1 cm. The flap of scalp was turned forward, disclosing a turgid, rounded mass in the pericranium. The pericranium was incised to the bone close to the margin of the tumor. Several arteries in the pericranium crossing the margin of the tumor required clamps. The tumor was cautiously elevated until several narrow vessels were seen passing from its inferior surface into orifices in the cranium. Ligation of these delicate vessels was impracticable, and the entire mass was quickly stripped off the bone. This procedure left about ten small actively bleeding veins. All bleeding was stopped by electrocoagulation. The bone under the tumor presented an oval depression exactly corresponding to the size of the tumor. The floor of

the depression was flat and apparently on a level with the inner table, as the depth of the depression was about the estimated thickness of the outer table and diploe. The margin of the depression was smooth. The outer table of the surrounding normal bone merely shelved down abruptly to become continuous with the floor, which was sieve-like by virtue of about ten foramina each of which was occupied by the stump of a delicate vein. The flap of scalp was sutured in place without drainage. Recovery was uneventful. The scar was inconspicuous. In January, 1924, the patient reported that there had not been a recurrence of the tumor or of the symptoms which were associated with it.

*Pathological Study of the Tumor*—The gross specimen was a disk of spongy tissue about 5 cm in diameter and 0.5 cm thick. One surface, the upper or outer, was velvety and pink, resembling areolar tissue. The obverse surface, which was applied to the bone, consisted of a thin, tough, white membrane. When this



Fig 1—Front view of patient with head erect

membrane was stretched, ten orifices about 1 mm in diameter became apparent. These orifices led into cavernous spaces immediately under the white membrane. The spaces were traversed by delicate septums which merged into the spongy tissue, making up most of the thickness of the disk. In cross-section, this spongy zone was seen to contain numerous small vessels of moderately thick walls.

Microscopic sections showed three merging zones. The one corresponding to the tough, white membrane was a layer of dense avascular connective tissue. Delicate partitions of connective tissue extended from it into the middle zone, which consisted largely of irregular sinuses lined by endothelium. Serial sections established the fact that these sinuses communicated with each other. Some of the partitions between the sinuses were provided with abundant small vessels. The zone corresponding to the pink velvety surface of the specimen was composed of this vascular connective tissue, which in this situation was more dense than in the middle zone and not interrupted by sinuses. A section through one of the orifices in the tough, white membrane showed merely a gap in the avascular zone.

Although the contour was smooth, the margins of this gap did not show any endothelium. The sinuses into which the gap opened, however, were provided with endothelium. It was probable that the endothelial lining in the region of the gap was stripped off and remained with the stumps of the emissary veins when the disk was peeled off the cranium.

Serial sections showed numerous instances of communication between small vessels of the connective tissue septums and the sinuses. Every communication was of capillary dimensions.

One series of sections showed a mass of granulation tissue protruding from the wall of a sinus. A sheet of fibrin and numerous granules of hemosiderin were associated with this mass, which apparently marked the site of a vascular accident a parietal thrombus or a hemorrhage into the areolar tissue adjacent to the sinus. Numerous communications could be demonstrated in the serial



Fig 2—Front view of patient with head bent forward

sections between the capillaries of the granulation tissue and the sinus into which it protruded

Sections stained to show elastic tissue revealed numerous elastic fibers in and about the walls of the sinuses. In many places, these elastic fibers were laid down circumferentially with respect to the sinuses. Some of the thinner septums did not contain elastic tissue, but most of the thicker ones contained much of it. The incidence of so much elastic tissue and its relation with the blood spaces are evidence in favor of the view that the entire lesion arose from previously existing blood vessels and not by organization and canalization of a hematoma. The pathologic diagnosis was "cavernous hemangioma of the pericranium."

#### PATHOLOGIC CONCEPTION OF SINUS PERICRAVIT

Much of the early literature on sinus pericranii was devoted to controversial discussion of the mode of origin. The earliest explanation was that of Stromeyer who assumed that a traumatic subperiosteal hema-

toma acquired communication with intracranial blood sinuses by way of torn emissary veins. This crude explanation was bolstered by later writers by assuming coincident fracture of the outer table of bone, by hypothecating some obscure interference with the coagulation mechanism and by unusual erosion of the skull bone by pachyomian granulations. Practically all of the authors saw the inadequacy of such mechanical theories when applied to cases of sinus pericranii occurring without a history of trauma and showing progressive growth. In order to render their theories tenable, these observers were required to distribute the cases in a classification which generally took the form of (a) traumatic cases, (b) spontaneous cases and (c) congenital cases. Still more complicated classifications based on structural peculiarities were elaborated.



Fig. 3—Side view of patient with head bent forward

The mechanical theory of formation was rather generally agreed to for the traumatic cases. The congenital cases were attributed to some "morbid conditions of the skull veins" such as "true angioma." The spontaneous cases were attributed to the development of a "varix" followed by pressure erosion of the skull. According to one theory, a rarefying osteitis is the primary lesion which leads to an alteration in the structure of the dural and pericranial vessels.

That the detailed classification of cases is unjustified is apparent from the fact that the structural characteristics of the specimens do not correspond with the groups separated from each other on an assumed etiologic basis. The angiomatous type of lesion is found as often in the traumatic group as in the congenital.

The foregoing criticism is made only with reference to cases following the typical course of sinus pericranii, by that I mean cases with a duration of months or years and in which gradual growth is apparent. It is true that there are recorded a few cases obviously due to gross trauma in which death occurred shortly after the injury and in which the lesion was primarily a fracture complicated by a hematoma communicating with an intracranial blood sinus. Such cases should not be included in the group "sinus pericranii", in fact, it was the inclusion of these cases which led to the over classification and the erroneous theories of origin.

Ernst Mueller<sup>4</sup> vigorously attacked the traumatic theory of origin, examining in detail the reports of twenty cases attributed to trauma by the authors of the reports. The histologic study of the specimen in

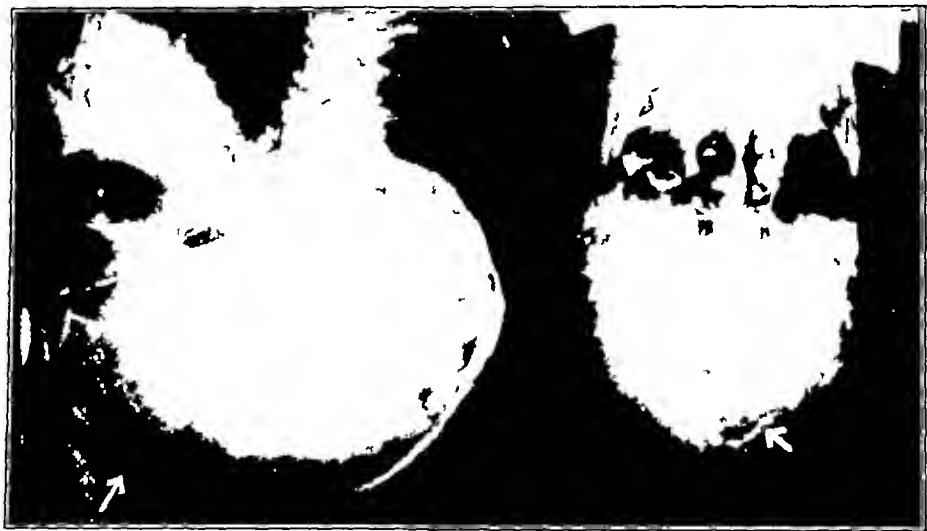


Fig 4—Roentgenogram of patient's skull. The apparent complete absence of bone in the lateral view at the point designated by the arrow is misleading, as a fenestrated plate of bone was demonstrated at operation

his own case convinced him that he was dealing with a true "cavernoma, a venous angioma." "On looking over the whole series of three groups (congenital, traumatic, and spontaneous) we find, discarding the large group in which no decision is possible, that the picture of varicose dilatation of subcutaneous skull veins or emissaries on the one hand, and hernial protrusions of the dural sinus on the other, is found in all groups. Angioma with the symptoms of sinus pericranii occurs congenitally and as a result of trauma. Such angiomas occur not only congenitally, but as Lannelongue points out, they may develop later."

<sup>4</sup> Mueller, Ernst Zur Frage des Sinus pericranii, Ztschr f ang Anat. 3 93, 1918



Achilles Mueller,<sup>5</sup> citing Lannelongue's similar opinions, concluded that most of the cases represented true angiomas "A traumatic origin in the sense of Stromeyer is unlikely and there is no proof of it"

Sudhoff<sup>6</sup> admitted the plausibility of the traumatic explanation for the cases arising after gross trauma, but left the inference that he agreed with Demme<sup>7</sup> that the congenital cases were due to "genuine varix" communicating with intracranial sinuses Mastin ascribed most of the cases he collected to "angioma"

I am convinced that all the cases of typical sinus pericranii, that is, cases with an extended duration and a reasonably long period of gradual development, are characterized by a lesion of the structural type of hemangioma The hemangioma in a case of sinus pericranii is exceptional only because of its special relations These special relations con-

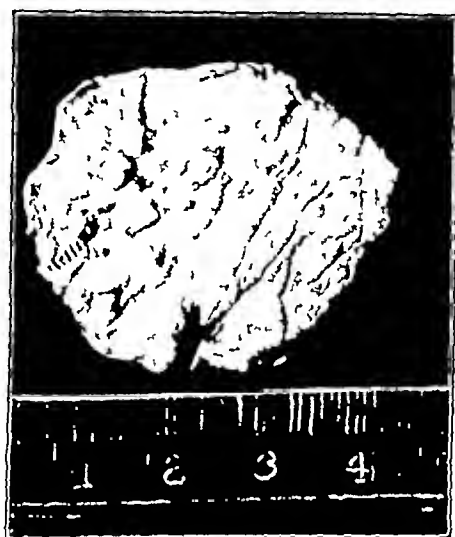


Fig 5—The gross specimen The surface shown is the one which was applied to the skull The minute orifices left by the avulsion of the emissary veins are barely visible Most of them are obscured by the wrinkles in which they lie

sist of a communication with the dural sinuses by way of emissary veins on the one hand, and with vessels of the pericranium on the other hand

I see no reason for separating the "spontaneous" cases from the "traumatic" In the latter, the trauma is frequently trivial, and in the spontaneous cases, similar trauma may easily have been unnoticed or forgotten Even some of the "congenital" cases may have been traumatic,

5 Mueller, Achilles Ueber Sinus pericranii, Berl klin Wchnschr **49** 1372, 1912

6 Sudhoff, Walther Ueber eine neue einfache Operationsmethode des Sinus pericranii, Deutsche Ztschr f Chir **186** 98, 1924

7 Demme, Hermann Ueber extracranielle mit den Sinus durae matris communicirende Blutcysten, Virchows Arch f path Anat **23** 48, 1862

although it is undisputed that a hemangioma or varix can arise as a result of a defect of development in the common anlage of arteries and veins

# CONCEPTION OF SINUS PERICRANII (AND OTHER SIMPLE HEMANGIOMAS) AS AN ANOMALY RESULTING FROM ABNORMAL ARTERIOVENOUS COMMUNICATIONS

The origin of sinus pericrani is explained by identifying the lesion with hemangioma only for those who are satisfied with the traditional concept of hemangioma as a neoplastic entity. Mont Reid's advanced excellent reasons for abandoning the occult concept of neoplasia with reference to simple hemangiomas, which he believes are the result of

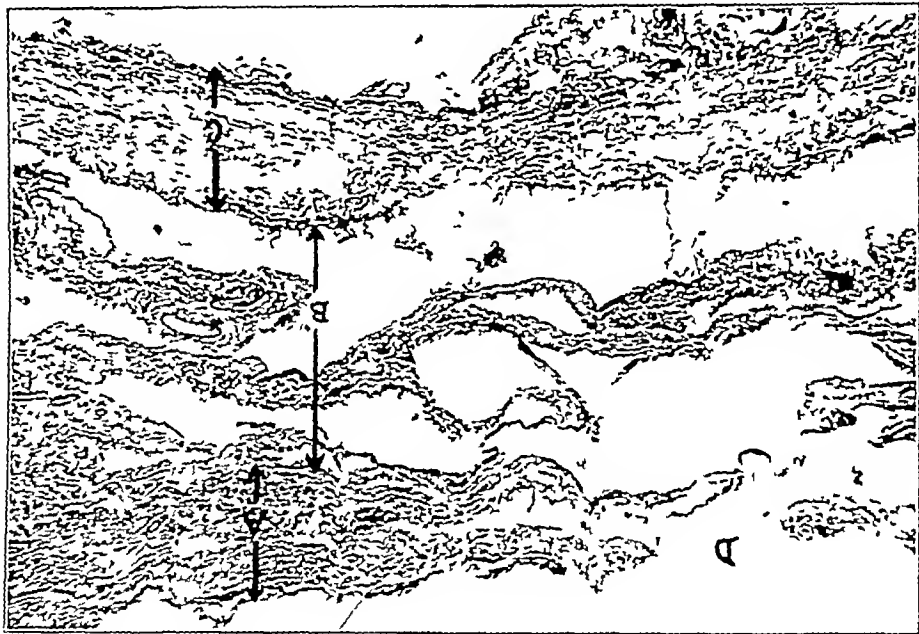


Fig 6—Low power photomicrograph of a cross-section of the specimen. *A* indicates the avascular membrane which was applied to the skull, *B* the middle zone of cavernous spaces, *C*, the vascularized zone forming the upper surface of the tumor, *D*, the gap representing the orifice left by the avulsion of a vein penetrating the cranial bone

abnormal arteriovenous communications. Simple hemangioma does not bear a resemblance to true neoplasms which are characterized by a proliferation of cells as units. It is true that there are vascular tumors of progressive growth which are attended by marked proliferation of endothelial cells, but these lesions are excluded from the simple hemangiomas and called hemangio-endotheliomas to designate their blastomatous character. The frequency with which trauma antedates the

development of a hemangioma suggests a mechanical cause. The regional incidence of hemangioma corresponds to a traumatic theory of origin, for it occurs most frequently where soft parts are easily compressed between a blunt object and underlying bone. It is true that hemangiomas appear to grow as do neoplasms. Reid has shown similar progressive growth of a restricted part of the vascular bed as a result of experimentally produced arteriovenous fistules. Most convincing of all the

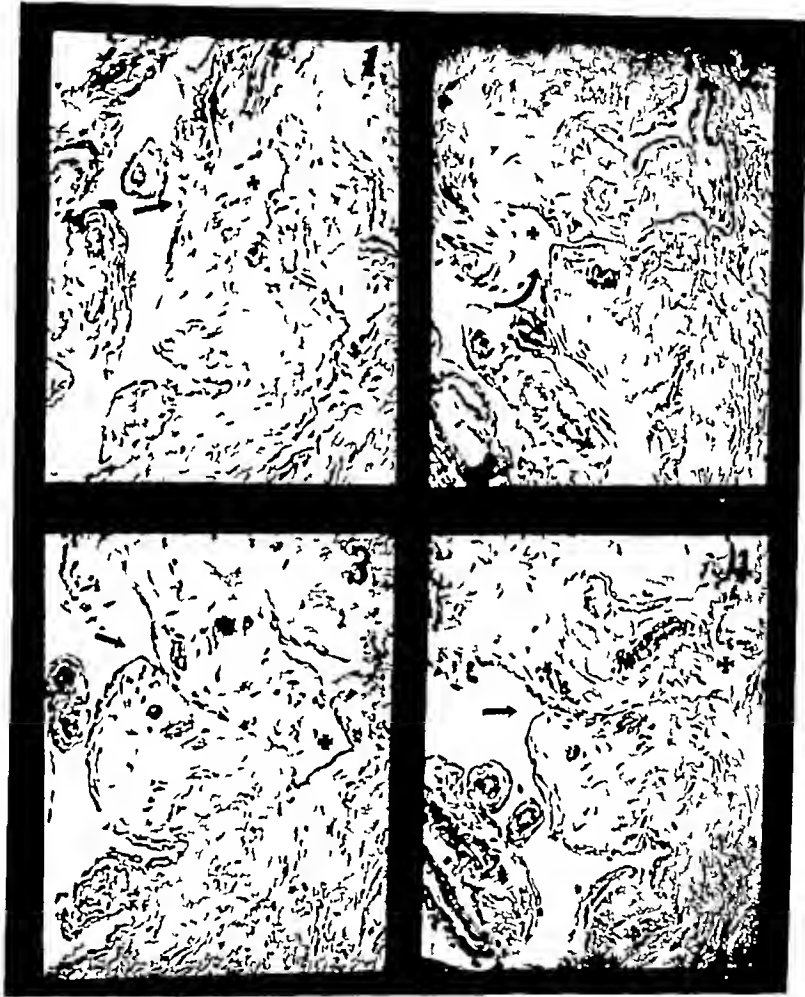


Fig 7—Four sections from a series, showing the communication between a cavernous space and a group of vessels in the adjoining connective tissue partition. The arrows mark the cavernous space. The crosses mark the network of vessels.

evidence is the finding of arteriovenous communications in progressively growing hemangiomas.

So far as I am able to ascertain, no writer has considered the possibility that sinus pericranii is caused by the formation of abnormal arteriovenous communications. If this thesis can be sustained, Reid's belief will have received additional support in view of the typical hemangiomatous structure of the tumor in sinus pericranii.

Certain features in the case reported, as well as similar observations recorded in the literature, favor the view that the hemangioma is caused by arteriovenous fistulas. Blood vessels radiating around the lesion in the pericranium required clamping when the tumor was resected. These were not large or tortuous, nevertheless, they provided communication between the hemangioma and the surrounding peripheral circulation. The specimen, as noted in the pathologic description, showed numerous instances of direct communication between the small vessels of the septums and the cavernous spaces. Further, the capillaries of the granulation tissue arising from the wall of one of the cavernous spaces opened freely into the space. The presence and the arrangement of the elastic



Fig 8—Section through the patch of granulation tissue. The arrow lies in a cavernous space and points toward an opening into the capillary system of the granulation tissue

fibers of the tumor mass indicated its origin from previously existing blood vessels

The absence of thrill and bruit may be cited as evidence against this theory. Some of the reported cases, as the one reported by Derrne, however, were characterized by thrill and bruit. In those which do not present these physical signs, one needs merely to assume that the arterial communications are of small caliber

My view of sinus pericranii, then, is that insignificant trauma may cause abnormal communications between small arteries of the pericranium and emissary veins. Once established, these fistulas cause dilatation and tortuosity of the veins subjected to the abnormal pressure

Gradually other fistulas are formed as the walls of the vein become attenuated and as the arterial elements dilate. In this manner, a congeries of vascular channels is built in which it is impossible to distinguish arteries from veins. The dilatation of the emissary veins extends to the adjacent diploic veins, and the bone of the cranium gradually undergoes absorption as a result of the constant pressure of the vascular lesion. The communication with the intracranial sinus is not an anomalous condition, in fact, the communication existed by way of the diploic veins and minute emissaries before the "aneurysm by anastomosis" became established. The single and essential element in the etiology of the lesion is

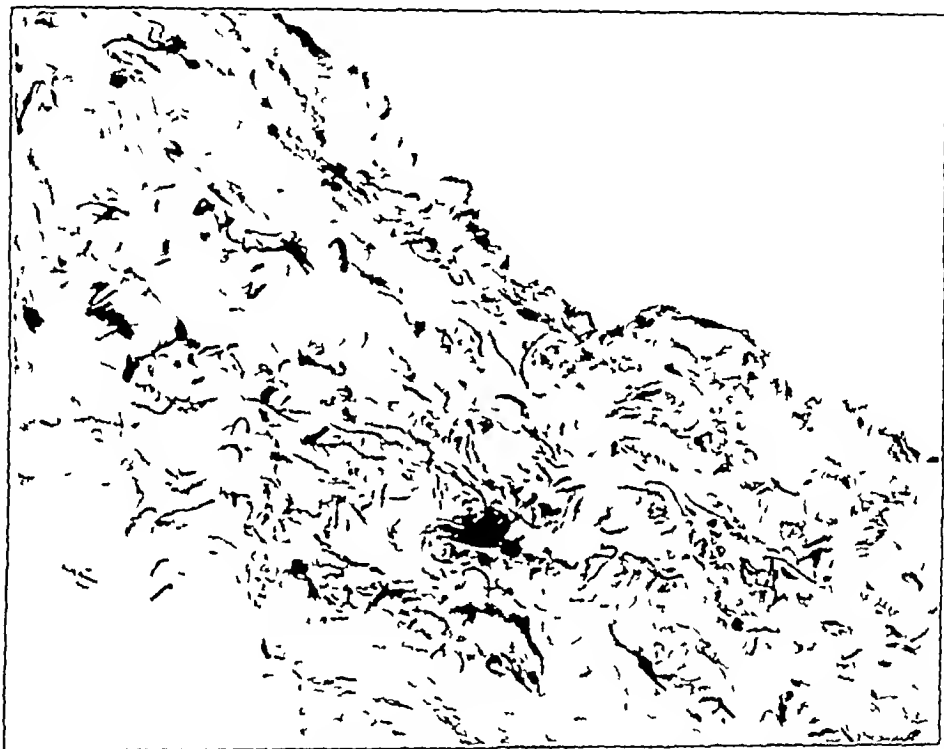


Fig 9—Section of the wall of one of the cavernous spaces, stained for elastic tissue. The black lines represent elastic fibers.

the transmission of arterial blood velocity and pressure into the emissary veins or into veins communicating with them. Such abnormal communications might arise congenitally as a result of faulty development of the arteriovenous anlage, but most of the cases are doubtless traumatic in origin.

#### TECHNICAL POINTS IN THE SURGICAL TREATMENT OF SINUS PERICRANII

The chief consideration in devising operative methods for the treatment of patients with sinus pericranii has been to avoid dangerous or fatal hemorrhage. Some operators have been led to employ extensive craniotomies in order to deal safely with large vessels running through

the cranium and communicating with the longitudinal sinus. When the pedicle vein is large, doubtless through exposure is an element of safety. Wooden pegs, ivory pegs, and plugs of wax have been employed for the occlusion of small foramina, all with some success. Dr. Gatch and myself conceived that electrocoagulation would secure ideal hemostasis as the emissary veins were of small caliber. The result in every way justified our expectation. We considered that rigid occlusion of the foramina is unnecessary, as the lesion is permanently healed by the resection of the central mass of arteriovenous fistulas. The method we employed has the advantage of leaving no foreign substance in the tissues and the desirable feature of speed and certainty. Electrocoagulation may prove to be a valuable adjunct in all craniotomies which are often attended by obstinate bleeding from emissary veins and diploic vessels.

## SUMMARY

1 "Sinus perrami" is the term best adapted by reason of historical connections to designate a hemangioma of the perramium communicating with intracranial blood sinuses and characterized by distinctive symptoms.

2 A patient with sinus perrami of traumatic origin is reported as cured by resection of the extracranial hemangioma.

3 The use of electrocoagulation to control bleeding of emissary veins is reported.

4 Arteriovenous communications of capillary dimensions were demonstrated in the specimen obtained at operation. Such communications provide a dynamic explanation of the origin of sinus perrami.

5 Histologic evidence that the hemangioma in this case was due to abnormal arteriovenous communications is interpreted as reinforcing Reid's conclusions that all simple hemangiomas are of such origin.

# CHRONIC APPENDICITIS \*

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It is common knowledge that many abdominal explorations made after chronic appendicitis has been diagnosed have revealed an insufficient pathologic process to warrant the section, and that the patients, after removal of the appendix, have been discharged without any relief from primary symptoms and perhaps, subjectively, in a worse condition than before the operation. So much has been said and written about the commission of such errors in diagnosis that the pendulum has swung the other way, and many physicians refuse to acknowledge the presence of a condition that might properly be termed chronic appendicitis.

The statement that there is no such entity as chronic appendicitis, even if based only on clinical experience, would warrant consideration, but the claim that there is no pathologic basis for the use of the term merits the most careful investigation before such a statement be accepted. To obtain the proper conception and the proper evaluation of the data it is necessary to correlate the clinical and the pathologic observations.

The clinical history and signs play the minor rôle in the final analysis. A study of the microscopic changes in the tissues is as near an approach to the physical basis as is at present obtainable. While the interpretation of a section of tissue is subject to the "personal equation" variation of opinion, on the whole, the microscopic picture of chronic inflammation is well established, and the disturbances and processes termed chronic inflammation in general pathology are found to vary but little when studied in special organs. Therefore, in conformation with the method employed in other problems, the pathologic picture, gross and microscopic, must be accepted as final. Then, if the clinical signs do not accord with the diagnosis, either there have been errors in observation and interpretation or diagnostic aids of greater precision should be sought.

From Sept 8, 1922, to Feb 1, 1927, I performed 1,087 abdominal sections for appendicitis, ninety-two of which were performed after a preoperative diagnosis of chronic appendicitis had been made. A personal study of the ninety-two patients from a clinical and pathologic standpoint furnishes the subject matter of this paper. Clinical and pathologic observations concerning many appendixes removed in the course of some other operation are also contributed. It is hoped that this study may result in so changing the nomenclature of certain clinical and pathologic conditions referable to the appendix as to make it

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\* From the surgical service of the Brownsville and East New York Hospital

possible for those who aver and those who deny the existence of "chronic appendicitis" to meet on common ground and to speak a similar and mutually intelligible language. The great diversity of opinion on the existence of such an entity as "chronic appendicitis" and the great variation in the criteria used by the proponents to define the pathologic picture of this disease shows that such a result is desirable. Dr A A Eisenberg, the pathologist of the institution in which this study was made, showed me twenty answers to a questionnaire sent to the most prominent clinicians in the United States, in which, among other inquiries, was one regarding the microscopic picture of what was termed chronic appendicitis. No two answers were similar and all were contradictory. These confusing results helped to stimulate this study.

No attempt will be made to discuss the details of diagnosis of chronic appendicular disease. It is definitely believed that the correct diagnosis of this condition should invariably be a result of the exclusion of all other possible diseases. All of these cases were thoroughly investigated before operation and due attention was paid to the possibility that some other lesion might be responsible for the symptoms of which the patient complained. Cystoscopy, ureteral catheterization and pyelography are procedures not to be rashly and indiscriminately prescribed, but in cases of chronic appendicitis such routine examination is recommended. In these cases it was only after other conditions had been excluded by these methods that chronic appendicitis was diagnosed and that operation for this disease was advised.

Of the ninety-two cases in which operation was performed fifty-one were diagnosed microscopically as chronic productive appendicitis, twenty-seven as fibrosis of the appendix, eleven as chronic obliterative appendicitis and two as normal. Before proceeding to analyze the data it is important to define the terms used, to distinguish between chronic inflammation and fibrosis of the appendix, and to describe their pathogenesis.

Briefly, inflammation is the name given to describe the immediate protective and defensive local reaction to an injury. Its aim seems to be the prevention of further injuries by antagonizing the injurious agent and causing a solution and removal of foreign materials, which includes the dead tissue or cellular debris, it is distinct from the process of repair, although frequently the processes overlap and cause confusion by proceeding simultaneously in the same areas. Extensive injuries that cause metabolic disturbances in cells may not arouse any inflammatory reaction. Undue pressure exerted on cells may cause a slow destruction with little or no inflammatory reaction as for instance, in the hydronephrotic kidney. On the other hand, an injury which may



be scarcely visible, the death of a few cells and their coagulation into what might be termed a foreign body or the introduction of a foreign body may start an intense inflammatory reaction

The phenomena of acute inflammation are familiar, namely early contraction followed by dilatation of the vessels accompanied by flushing and local increase in temperature, the slowing of the blood stream, margination of the leukocytes, emigration of these cells, diapedesis and the exit of the red cells and exudation of the fluid from the blood vessels, which causes edema, and coagulation of the fluid resulting from the action of thrombokinase-forming fibrin. These changes are followed by the destruction of the invading agent, the autolysis of the dead tissue and its liquefaction, partial digestion by leukocytes, partial absorption by the lymphatics and the repair of the gaps

Living cells possess the ability to assimilate nutrition, as evinced by an increase of protoplasmic mass. As the mass becomes larger, the absorbing surface increases in area, but not proportionately, and ultimately the surface is not sufficiently great to provide adequate nourishment. The division of the protoplasm and nucleus occur with the formation of the two similar cells to replace the old one.

When an injury occurs to a tissue or an organ, a stimulus is furnished or an inhibition removed, which results in a more rapid division of the remaining uninjured cells in the attempt to provide an adequate amount of functioning tissue.

The various tissues of the body have an inherent specificity of regeneration in contradistinction to the embryonal cells. This specialization is rigid except in the case of connective tissue, in which greater latitude exists. The rate of regeneration of tissue varies considerably, for example, the epidermis regenerates rapidly, while the central nervous system and striated muscle regenerate scarcely at all. Gaps formed in the latter by injury must be quickly filled in by some tissue which can restore continuity rapidly. Thus, because of the different rates and powers of regeneration of various tissues, local repair is sometimes carried out by the injured organ-substance itself, it is, however, more often carried out by the inferior material, connective tissue. But even though such patching occurs, there is almost always an attempt there or elsewhere to restore the original specialized tissue unless it has been entirely destroyed.

The epithelium of the mucous membranes regenerates with remarkable ease and rapidity, growing out from the edges by mitotic division to cover smoothly any denuded area. The glands are reproduced from the remaining specialized cells.

Connective tissue reproduces itself in great profusion by rapid sheetlike cell division. At first, these newly formed cells lie loosely in the replacement site, later, their cytoplasmic fibrils become arranged

more definitely in a parallel formation, and they become compact and so conspicuous that they often efface the other characteristics of the cells, the final result being the formation of scar tissue.

Smooth muscle has little tendency toward regeneration. Wounds resulting in loss of substance are healed by bridging with connective tissue which, after having passed through the stages just described, contracts and diminishes the size of the gap.

If an acute invasion by a pyogenic organism occurs in an organ such as the appendix, hyperemia, leukocytic invasion, destruction of the invading agent and considerable tissue, autolysis and liquefaction of the latter result. Debridement by partial leukocytic digestion and partial absorption through the lymphatics follows, and the gap is repaired. The mucosa may become completely regenerated, or some fibrosis may result. The submucous fibrous tissue increases. If the muscle walls have been involved, they show evidences of replacement by fibrous tissue.

If the process is not fulminating, if the protecting influences gain the upper hand, and if the irritation persists in a milder degree because it is not entirely neutralized or removed, the infection becomes chronic. If the invading force consists of organisms, and if the balance between invader and defenders is struck at such a level that the organisms remain and continue to develop at a slow rate, they irritate the tissue and the reaction continues to be manifest, instead of being polymorphonuclear, however, the characteristic cells are lymphocytes, plasma cells and endothelial cells. The reparative processes result in fibrous deposits and thickening. There is no redness or heat, but swelling may be present. The most prominent pathologic feature is the abundant formation of new connective tissue and the round cell infiltration.

The inflammation may be chronic from the beginning, as for instance in the case of the introduction of a foreign body into the tissues or as a result of infection by organisms which act slowly on the tissues, e. g. tuberculosis syphilis and actinomycosis.

It becomes apparent, then, that a distinction must be drawn between the terminal fibrosis of a single or of repeated attacks of acute inflammation and of a true chronic inflammation. A true chronic inflammation is characterized not only by the presence of the fibrosis, but also by the presence of lymphocytes, endothelial cells and plasma cells. The fibrosis of the acute attacks is a termination, an end-result, the battle is over, the reaction is completed and the irritant is no longer active. In the chronic inflammation, the process is still active, with the reaction in progress and the irritant still injurious to the tissues. Failure to distinguish between these two conditions has led to much confusion. It is incorrect to call a terminal fibrosis a chronic inflammation on the other hand one cannot deny the possibility of chronic appendicitis.

because terminal fibrosis has incorrectly been designated as this condition in many instances

In this study, the criteria on which the diagnosis of chronic appendicitis is based are distention of the capillaries with an increase in leukocytic content, the presence of eosinophils in the muscle bundles, fibrosis, particularly that seen between the bundles of the inner circular muscular layer, thickening of the serosa, small lakes of round cells, general round cell infiltration and increase in endothelial cells. These may be present in any combination. The sections of some appendixes show massive granulations of the serosa with typical granulation tissue of the kind commonly seen in the presence of chronic inflammatory reaction.

The sections in the photomicrographs show the pathologic alterations in the cells which take place in cases of chronic appendicitis. Figure 4 shows the section of an appendix taken from a child, aged 16. It might be said that a child of 16 has scarcely lived long enough to develop a chronic inflammation of the appendix, but it must be remembered that acute appendicitis is a disease of early life, and that where it is possible for an acute inflammation to develop, it is possible for the chronic condition to persist when the proper balance is struck between the invading and the defensive forces.

The cases illustrated by the photomicrographs are different from those classified as chronic obliterative appendicitis. The latter condition is characterized by replacement in greater or less degree of all the layers of the organ by fibrous connective tissue and the obliteration of the lumen by granulation tissue, which subsequently becomes organized. Scarring is predominant, and when the process is complete, signs of activity are not seen. Before the end-stage, however, activity may be noted. Eleven of the ninety-two cases in which operation was performed were of this type. All of the patients were less than 40 years of age, and all gave a history of repeated attacks of symptoms, but only four recalled having more than three attacks. The tremendous fibrous replacement in the cases in which there were only a few attacks and the fact that the patients were under the age of 40 do not support the views of Zuckerkandl<sup>1</sup> and Ribbert<sup>2</sup>.

It has been claimed that fibrosis may occur without previous inflammation. Ribbert<sup>2</sup> and Zuckerkandl<sup>1</sup> regard fibrosis as an atrophic retrogressive process associated with advancing age and particularly liable to occur in a vestigial organ such as the appendix. This, however, has been heatedly contested. Aschoff<sup>3</sup> affirms that fibrosis is evidence

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1 Zuckerkandl *Anat. Hefte*, 1894, vol. 4

2 Ribbert *Virchows Arch. f. path. Anat.*, 1893, vol. 132

3 Aschoff, L. *Die Wormfortsatzentzündung*, 1908

of a previously existent inflammation Ribbert and Zuckerkandl, however, fail to reconcile the tremendous fibrosis frequently seen in appendixes of children and young adults with their view on the atrophic retrogressive changes related to advancing age. One of the reasons for this controversy is the difficulty in understanding why many appendixes which were removed in the course of some other operation, and which histologically showed marked replacement of the wall by fibrous tissue,

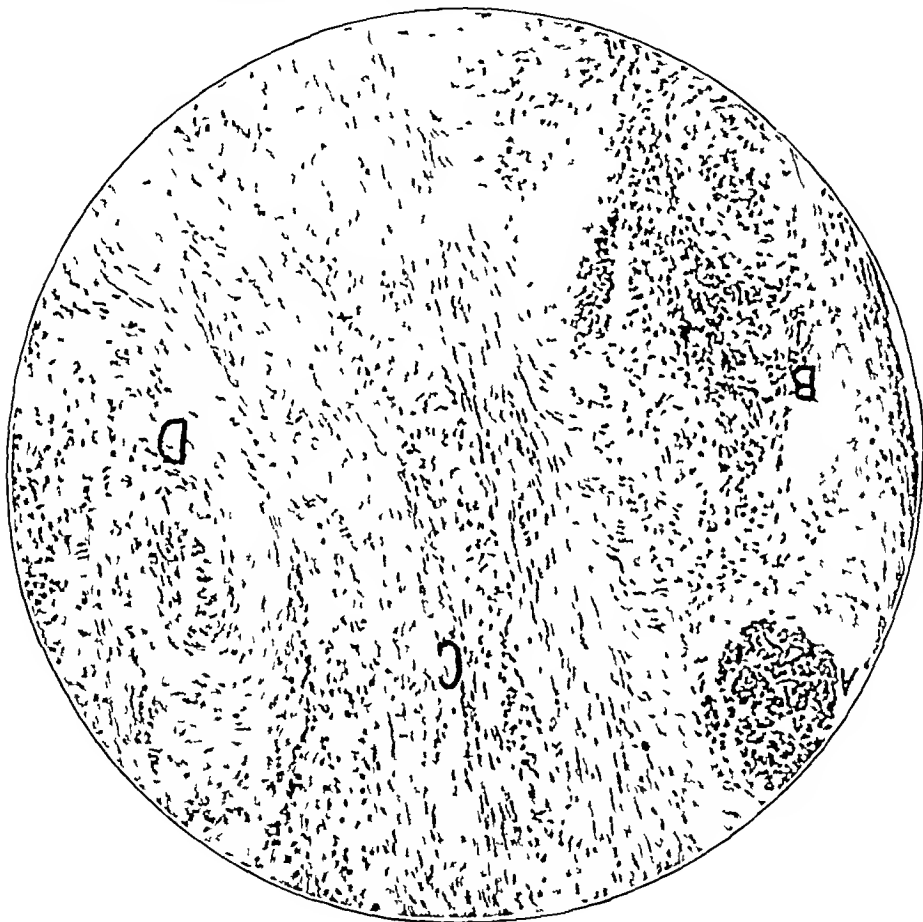


Fig 1—A section of an appendix, which is typical of the type of activity termed chronic inflammation,  $\times 90$ . A indicates a "lake" of round cells in the serosa, and B, a less concentrated infiltration of the serosa by similar cells. The inner circular muscular layer at C is undergoing replacement fibrosis and is infiltrated with small round cells. The submucosa D also shows marked fibrosis and round cell deposit.

apparently did not produce disturbances which would point, clinically, to a pathologic organ. Williams and Slater,<sup>4</sup> in a study of appendices removed as a routine during pelvic operative procedures, report the frequent occurrence of fibrosis, although the patient had not com-

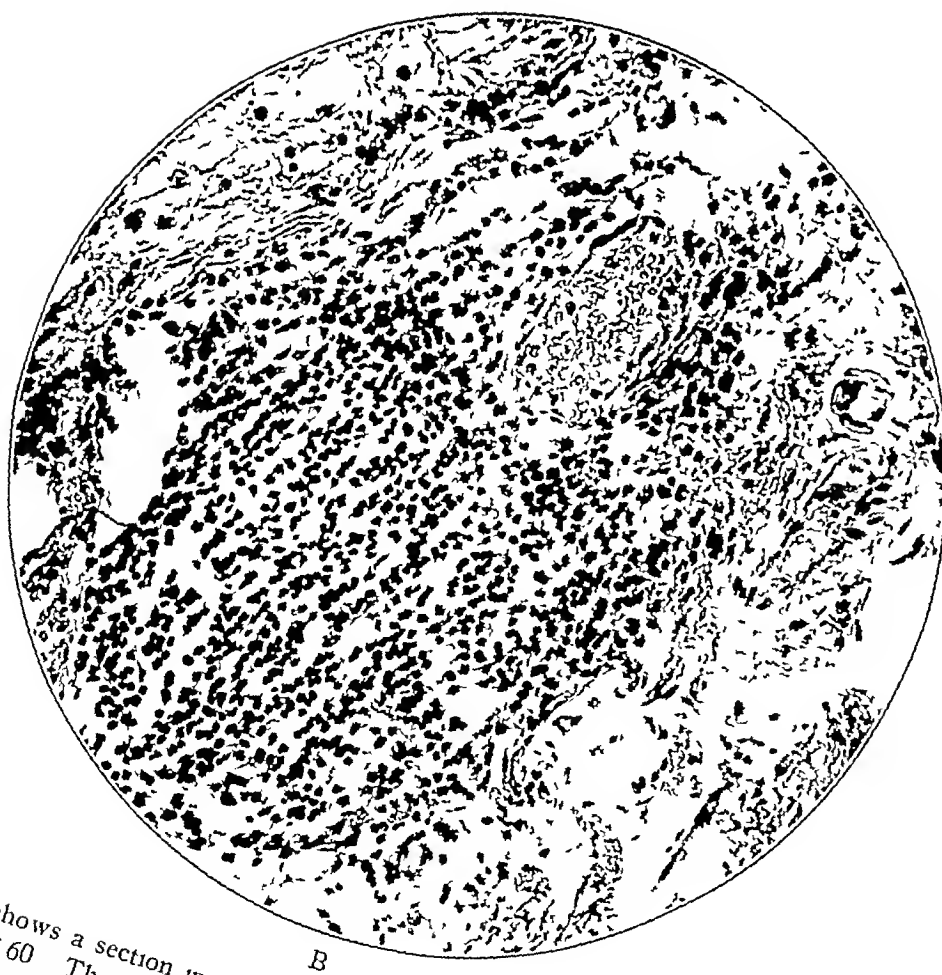
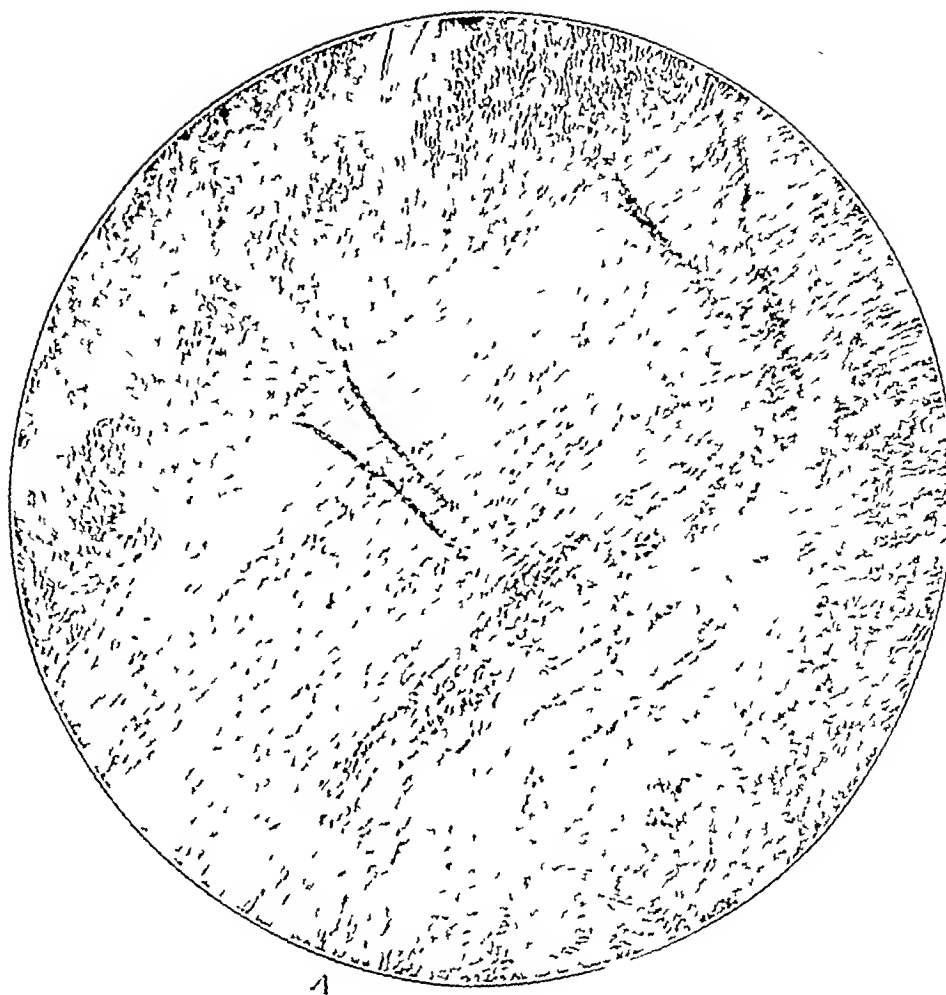


Fig 2—*A* shows a section in which the serosa is practically a mass of granulation tissue,  $\times 60$ . The muscle bundles are separated by fibrous tissue deposit. The higher magnification in *B* shows lymphocytic infiltration of the serosa which is characteristic of low grade inflammatory reactions.

plained of symptoms referable to the appendix. Another reason is that it may be difficult to understand how an appendix in which the normal structures have been almost entirely replaced by fibrous tissue can be productive of symptoms. These questions will be considered later.

Accompanying the appendiceal inflammation is a greater or less degree of periappendicitis, i. e., an inflammatory reaction by contiguity of the adjacent intestines and peritoneum, accompanied by a serous exudate and some coagulation of the fluid-producing fibrin which may

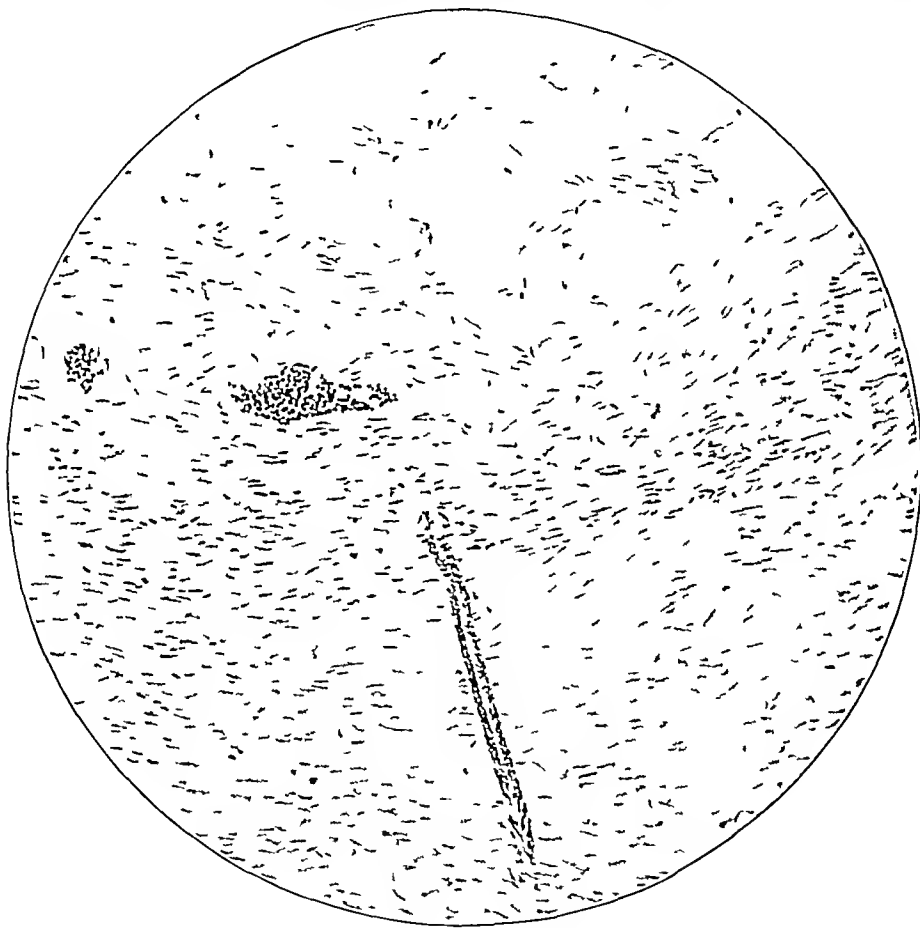
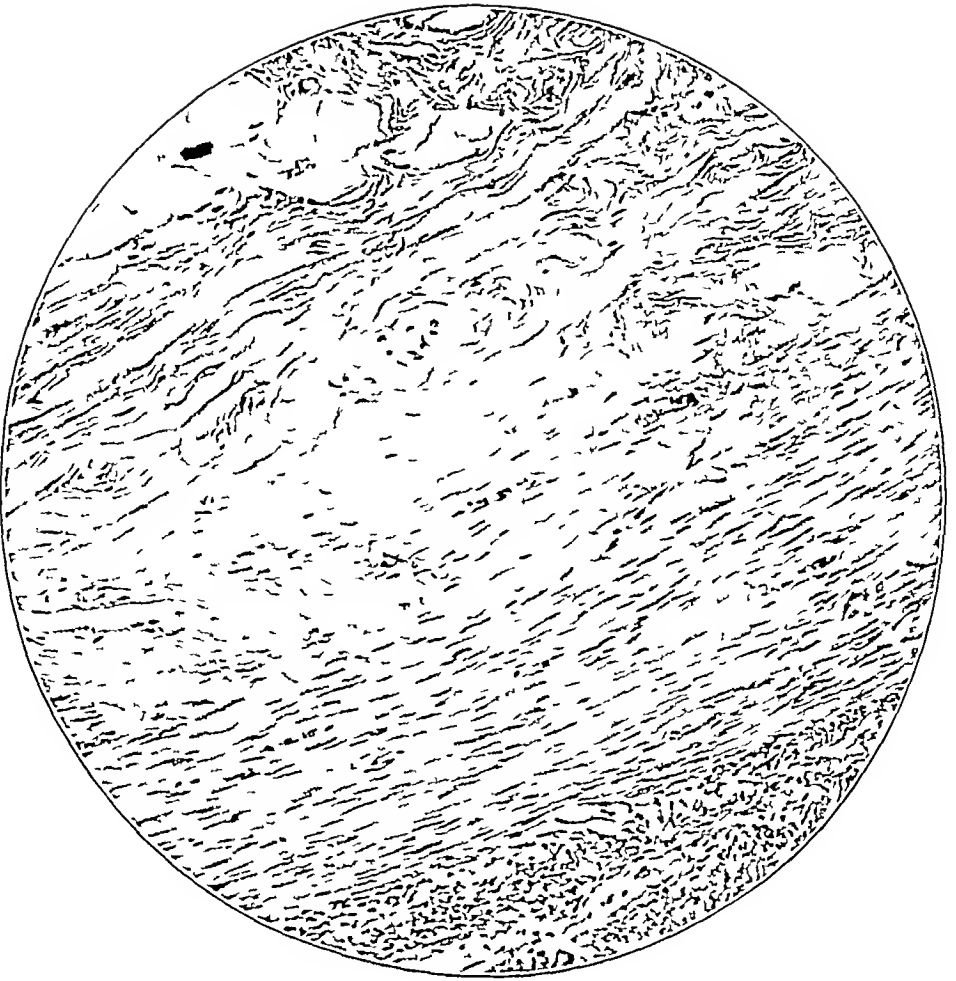


Fig 3—Marked fibrosis of the submucosa separation of the muscular fibres by connective tissue and lakes of round cells denoting a concentration of activity,  $\times 90$ . Sections of this kind cannot be classified as belonging to cases of terminal fibrosis. In the latter, the condition is one of scarring only, no activity is to be seen. The predominating feature is connective tissue replacement.

and frequently does act as a cementing substance to fix the appendix in all sorts of twisted positions to the cecum, ileum, parietal peritoneum bladder, fallopian tube omentum and other adjacent parts. Later granting defensive forces there is more or less organization of these adhesions with corresponding distortion of the appendiceal tube and limitation of the motion of the organ. The remaining adhesions may



A



B

Fig 4—A shows “granulation tissue” serosa, and marked connective tissue replacement,  $\times 200$  The appendix from which this section was cut was removed from a child, aged 16 B is the same section under higher magnification

be only fine, vellimentous and elastic, they may be thick dense and unyielding, or they show innumerable gradations between these extremes

The appendix is a cecal diverticulum formed of all the coats of the intestine. It hangs from the cecum, being attached by a peritoneal fold of varying size. The appendix hangs freely or is thrown into coils, depending on the size and shape of this fold. Normally, there is no



Fig 5—A high magnification of a section showing tremendous fibrosis and round cell deposit in the muscularis of the appendix of child, aged 11,  $\times 200$

kinking of the appendix, and the lumen remains patent throughout, insuring free drainage of the secretions and contents. When periapendicular adhesions occur, one of the most common results is kinking of the appendiceal tube which causes interference with free drainage of the contents. Stasis results, the severity of which corresponds to the degree of obstruction offered by the kink. This stoppage, in turn, provides the necessary factor for infection. Periapendicular adhesions frequently angulate or twist the meso-appendix so as to interfere mechanically with the venous flow such stasis further



favors the infection. Jones and Evans<sup>5</sup> stress this point in discussions of the cause of appendicitis. It is understood that the degree of infection is modified by other factors, such as, virulence and the number of invading organisms, amount of stasis, the suddenness with which the stasis is effected, the resistance of the host and other factors. A sudden and complete obstruction, such as might be offered by the impingement of a fecolith against a well developed valve of Gerlach, would cause a severe appendicitis, with rapid and progressive involvement of all the coats. The organ becomes a huge bouillon culture of bacteria which begin traversing the walls. The walls quickly become so distended that the flow of blood is stopped, and gangrene and perforation soon result. On the other hand, if the other factors were not modified, and if a mild degree of stasis were to be occasioned by partial obliteration of the lumen at one point as a result of a kink, a low grade inflammation might occur, because of the mechanical derangement, this inflammation would continue indefinitely.

Thirty-nine of the ninety-two patients who were operated on had symptoms of less than one year's duration. The longest period during which symptoms had existed was eighteen years. All the patients had pain in the right lower quadrant of the abdomen.

At operation, twenty-seven appendices were found to occupy a retrocecal position. This is at variance with the observations of Gladstone and Wakely<sup>6</sup> who note a retrocecal position of the appendix in 2,076 instances out of 3,000 necropsies. The retrocecal position of the appendix in itself favors stasis and inflammation because of the tendency toward angulation at the base, particularly when the cecum is filled. This point has previously been stressed by Jones and Evans<sup>5</sup> in a discussion of the mechanical factors causing appendicitis.

Kinks of the appendix were found in eighteen instances. These were noted only when they were so well marked that they could be considered to hinder the easy emptying of the organ. The kinks were occasioned by adhesions of the appendix to the lateral pelvic wall, the cecum or ileum. Adhesions of the appendix were noted in fifty-four instances. These were of all degrees and gradations, from fine, easily formed webs to well organized and, in one instance, calcified fibrous bands.

A continued low grade infection such as that previously described results in continued replacement of the original wall by fibrous tissue. Such an organ may produce several types of symptoms: (1) symptoms referable to the organ itself, (2) symptoms resulting from parietal

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5 Jones and Evans, E. J. L. *Practitioner* **114** 113 (Feb.) 1925

6 Gladstone, R. J. and Wakely, C. P. C. *Brit. J. Surg.* **2** 503 (Jan.) 1924

peritoneal irritation and (3) symptoms resulting from disturbances in physiologically and anatomically related organs

One of the most common manifestations of disease in an organ is a disturbance in function. The diagnosis of chronic inflammation of the kidney, for instance is not dependent on the presence of pain in the composition of the blood plasma is impaired when it is diseased and the study of the disturbance of its function by investigating the quantitative alterations in some constituents of the plasma and urine and the symptoms occasioned by such alterations offers the key to the diagnosis. This holds true for other organs also

Most advances in physiologic knowledge relating to special organs have been gained by ablation of the organ and recognition of the resulting deficiency to the organism as a whole. The appendix considered as a vestigial organ, not having any ascertainable function or value, does not belong to the class described. Countless numbers of apparently normal appendices have been prophylactically removed in the course of another operation without any noticeable resulting deficiency. Its disorders cannot be studied from this point of view. Attention is not directed to its disorders by alteration in metabolism or by changes in special secretions of the body, but usually by the complaint of pain in the right lower quadrant of the abdomen

The Auerbach and Meissner plexus of nerves found in the stomach and small intestines are continued down into the appendix and are distributed in a similar fashion. Coming from the solar plexus and consisting of both mediated and nonmediated fibers from the cerebro-spinal and sympathetic systems, they pierce the outer longitudinal muscular layer. Between this and the inner circular layer they form the plexus of Auerbach which contains sympathetic ganglions of the peripheral variety. Then the nerves pass into the submucous layer where they form the plexus of Meissner. From here, nonmediated fibers (in conformation with sympathetic fiber distribution elsewhere in the body) are distributed to the mucosa as perigastric and sub-epithelial networks as well as to the muscular tissue. Centrally, these nerves reach the solar plexus from which impulses may reach the gangliated cord through the great splanchnic nerves arising from the sixth to the tenth dorsal ganglions. Thus the pathway of a nerve reflex involving the appendix is through fibers in the superior mesenteric plexus to the celiac plexus through the splanchnic nerves to the dorsal ganglions and through gray rami communicantes to the spinal cord

Peristaltic movements of the intestines are initiated by irritation of the intestinal mucosa. Unlike irritation on the surface of the body stimuli normally supplied to the intestinal mucosa by food are not transmitted to the cerebral cortex. The former are relayed to the brain for

the protection of the animal. Experience has taught that the latter are not injurious. As a result, cerebral coordination not being necessary, the stimuli are side-tracked in the cord, and the reflex arcs necessary to stimulate muscle fibers to peristaltic action or glands to secrete are completed. The stimuli from severe irritation to the appendiceal nerves, whether as a result of pressure or of inflammation, reach the cord and cre-

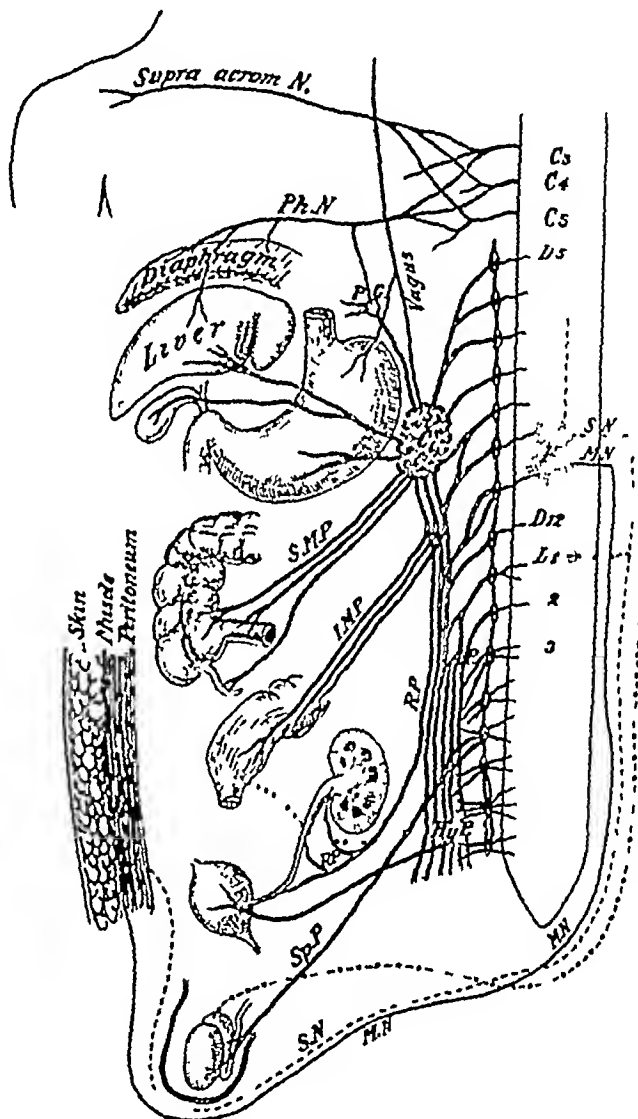


Fig 6—*Ph N* indicates the phrenic nerve, *P G*, the phrenic ganglion, *C*, the celiac or solar plexus, *S M P*, the superior mesenteric plexus, *I M P*, the inferior mesenteric plexus, *R P*, the renal plexus, *A P*, the aortic plexus, *Hyp P*, the hypogastric plexus, *Sp P*, the spermatic plexus, *C*, the cervical nerve roots, *D*, the dorsal nerve roots, *S N*, the sensory nerves, *M N*, the motor nerve, and *F*, the area of stimulation in the cord

ate a zone of hyperexcitability at the level of entrance (fig 6). This affects the adjacent sensory fibers so that impulses that were formerly subadequate to cause sensation now become adequate, and since the cortical perception is interpreted in terms of peripheral distribution, the sensation of

pain is appreciated at the sensory endings on the skin. When a severe stimulus is applied to a tissue of low sensibility which is in close central connection with a tissue of greater sensibility, the pain is referred to the latter rather than to the former. Through the sympathetic system, the spinal cord and the spinal sensory nerves the appendix is connected with a triangular area of the skin of the right side of the abdomen, the center of this area corresponds roughly to McBurney's point. The cause of this connection is the persistence in man of the segmental relationship between the cord, the skin and muscles, such as that found in primitive vertebrates. Irritation of sympathetic nerves resulting from inflammation of the wall of the appendix is similar to the irritation to the end-plates of sensory nerve caused by inflammation of the skin and subcutaneous tissue, in that the stimuli produced are of greater than normal magnitude. The stimuli of more than normal magnitude arising in the appendix may and do occasion pain on the surface of the body, generally near McBurney's point, because the cerebrum interprets the stimulus as having arisen from the cutaneous rather than from the visceral connection. Similar irritation may be produced by the pressure of unstriated muscle. The pain resulting from the contraction of a tubular structure like the cystic duct or the ureter, in the attempt to move a calculus, are examples of stimulation of the nerve by pressure of muscle contraction. Similar cramplike pains may also be produced by vigorous peristaltic movements of the appendiceal wall in an attempt to extrude a fecolith into the cecum. The analogy between the appendix and the ureter or the appendix and the cystic duct is not far-fetched. In either instance, the appendix, a tubular organ having muscular walls capable of vigorous contractions as shown by the segmentation of ingested barium, is compared to other tubular structures. The cystic duct has a far inferior musculature, and yet the colic resulting from the cystic obstruction is undoubtedly severe. That severe colic can be initiated by forceful peristaltic contractions of a ureter in which there is a kink or a stricture is undeniable. The possibility of similar colic in similar strictures must be granted. Strictures of the appendix do occur, it is not uncommon to find appendices with grossly recognizable annular diminution of wall and lumen caliber, as a result of either an annular fibrosis (the sequel to a previous acute inflammation) or of a constricting periaappendiceal adhesive band. In either instance, hyperperistaltic waves are initiated to overcome the tendency toward stasis and colic results. Pitzman states that in all cases of chronic appendicitis there are strictures that are patent between attacks. Fecoliths are more common in appendices which have been subjected to previous attacks and which are linked by adhesions or distorted by scar tissue. They are also more commonly encountered in those having

ptosis of the abdominal viscera, and in young persons chronically constipated. McWhorter<sup>8</sup> reports an operation for a pelvic condition, during which he examined the appendix, he found that it was normal and without palpable fecoliths, and did not excise it. Fourteen months later, the patient began to have definite short attacks of pain in the right lower quadrant, lasting from ten to fifteen minutes, followed by a dull ache and tenderness for the remainder of the day. There was no relation to food. The attacks were rarely absent for more than a week at a time, and were worse when the patient was constipated. One and a half years after the first operation, a second operation was performed for profuse persistent menorrhagia due to changes in the uterine wall, at this time, the appendix was found free, but the long artery near the tip was noticeably dilated, and there was a fecolith one-half inch (1.27 cm.) from the tip. He believed that this was strong evidence in favor of considering fecoliths as responsible for some cases of appendicular colic.

A considerable number of cases of so-called chronic appendicitis occurs in ptotic subjects. These ptotic sufferers have a dull steady, and sharp intermittent pain in the right lower quadrant of the abdomen. The colic is severe, and the patient is temporarily incapacitated. The excision of the appendix in these cases gives relief from the paroxysms of pain, but does not accomplish a cure, because it does not affect the concomittant conditions—ptosis, constipation and others—which have been important contributory factors in the production of the stasis necessary for fecolith formation, and for which the patient is often left untreated.

Pain may be produced by the tug of the appendix and adjacent cecum on the parietal peritoneum in those instances in which organization of adhesions has fixed the appendix and the cecum to the pelvic or abdominal wall after an acute inflammation with periappendicitis. Distention of the cecum or normal peristaltic movements during the churning process, especially if the ileocecal valve is competent, cause a tug on the adherent parietal peritoneum which produces pain. Experience with local anesthesia in abdominal operations has demonstrated a remarkable insensitiveness of the visceral peritoneum to cutting or burning, and, on the other hand, extreme sensitiveness of the parietal peritoneum to slight tugging.

The association of pylorospasm and gastric hyperacidity with chronic disease of the appendix has been thoroughly discussed in the literature on appendicitis. Much has been written on the frequency with which chronic inflammatory changes or the terminal fibrosis of repeated acute inflammations of the appendix has been found concurrently with chronic cholecystitis and cholelithiasis. It is not necessary to dwell on the reports of gastric hemorrhages cured by the removal of the appendix which

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<sup>8</sup> McWhorter, G. L. *S. Clin. N. Amer.* 4:713 (June) 1924.

histologically revealed little more than fibrosis of the muscular and sub-mucous layers with moderate lymphocytic infiltration. The names of Mayo, Moynihan, Deaver, Soltau, Fenwick, Sherren and others (men of wide experience and keen observation), have been associated with such reports. It has been exceedingly difficult in the past to imagine the possible relationship between the appendix and such remotely placed organs as the duodenum and gallbladder, but studies of the abdominal lymphatics have revealed the existence of morphologic connections which form a substantial basis for pathologic speculation. Reference is made to the work of Kodama,<sup>9</sup> who confirmed the existence of lymphatic connections (through the medium of the lymphatic gland situated at the beginning of the portal vein) between the appendix, duodenum, gallbladder and surface of the pancreas described by earlier workers. A direct route for the transmission of infection is thus established.

There is also a morphologic and physiologic connection between chronic appendicular disease and such conditions as pylorospasm or gastric hyperacidity. Stimuli from the appendix travel along the nerves accompanying the superior mesenteric artery to the celiac plexus which is a central receiving station for all abdominal viscera. From this point reflex arcs are completed with secretory glands or muscle-fibers of the appendix. When the stimuli are excessive both in number and intensity however, the impulses reaching the solar plexus radiate to other adjacent cells and complete reflex arcs through axons of the adjacent cells with for instance, the acid-producing cells of the stomach causing hypersecretion or with the muscle cells of the pylorus causing spasm.

Patients present themselves to physicians not because a pathologic diagnosis has been made, but because they experience pain or have what is manifest to them as abnormal reactions. They seek relief from their symptoms. These symptoms may be due directly to an organic lesion in the appendix, to functional derangements or to both together. Among the organic lesions are chronic inflammation, stricture, periaependiceal adhesions and kinks.

Colic similar in nature to ureteral or biliary colic may result from exaggerated peristaltic movements in the attempt to overcome stasis resulting from stricture or kinks or in the effort to expel a fecolith. Less severe pain may be occasioned in the cases of periaependiceal adhesions by the normal reverse peristaltic movements of the ascending colon, causing a tugging on the parietal peritoneum and thus stimulating the nerves in the subparietal peritoneal regions.

Acting as a focus an appendix which is the seat of a continued low grade inflammation may spread infection through lymphatic connections

(or through the blood stream) to the gallbladder, duodenal wall, pancreas and other organs

Through faulty radiation in the celiac plexus, impulses coming from appendixes such as those already described may be transmitted to nerve fibers which innervate glands or musculature in other organs

#### SUMMARY

This article has shown that dull aching pain or intermittent and colicky pain in the right lower quadrant of the abdomen may be referable to organic or to functional disturbances in the appendix, and from a purely pathologic basis it is not correct to group all the conditions of the appendix responsible for this pain under the heading "chronic appendicitis," nor is it fair to assume that unless appendixes show all the evidences of a chronic inflammation they cannot be the cause of the symptoms. It becomes evident that at least part of the basis for confusion and controversy has been the tendency to group a number of symptoms and to attribute their causation not only to one organ, but also to one type of lesion, namely, chronic inflammation, whereas in reality other etiologic factors may be involved. The term chronic appendicitis has not been applied to a pathologic picture by the average physician, but rather to a clinical picture, and in many of these cases the pathologist may not find any evidence of chronic inflammation, the symptoms having resulted from kinks adhesions and strictures. Until it will become possible to recognize a difference, clinically, between the symptoms produced by a chronic inflammation of the appendix and those produced by kinks, adhesions, strictures and other lesions, it is suggested that the term chronic appendicitis be discarded entirely by the clinician as a preoperative diagnostic cognomen, and that "appendicular colic" be substituted. The operative observations will furnish additional information for classification, and only the combined preoperative, operative and pathologic data will furnish the minimum requirements for a complete and accurate diagnosis.

It is understood that the term appendicular colic is satisfactory only as a working basis, as is ureteral colic, for instance, but at least it will have a definite meaning and a definite application.

The standardization of the criteria for the diagnosis of chronic inflammation is also an important necessity for the avoidance of further contradictions. As was mentioned previously, no two pathologists out of twenty questioned held the same views. This means that when the pathologist in Rochester says "chronic appendicitis," his colleague in Boston does not visualize a similar picture. The natural consequence has been confusion and controversy. With the acceptance of a definite criteria, such confusion will be avoided.

# PATHOGENESIS OF GOITER CONSIDERED AS ONE CONTINUOUS DISEASE PROCESS

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Much effort has been expended in the construction of a classification of the diseases of the thyroid gland which would be acceptable to the pathologist and surgeon. Each has worked largely from his own point of view. The result has been that the pathologist's product has been wholly inapplicable to the clinic and the practical man's product has paid scant attention to the requirements of scientific terminology. The most generally accepted classification divides goiters into the adolescent, the colloid, the nontoxic adenomas, the toxic adenomas and, finally, the exophthalmic type with or without eye signs. This classification has a certain advantage in that it emphasizes certain prominent clinical groups. It is faulty in that it suggests that these groups represent separate diseases, or at least, separate disease states. It is further at fault in that it employs pathologic terms of doubtful applicability and in part employs eponyms, always objectionable in scientific terminology. This combination is confusing and inaccurate.

In the investigation of any medical problem, the only class of persons with which one's theories must harmonize is the patients themselves. If they fit in a theory one need worry little about the opinion of other investigators. Though the following presentation is not in harmony with the results of other writers, it aligns itself with my clinical experience. In the attempt to correlate laboratory observations with the life histories of the patients among whom I have lived for a generation it has become more and more apparent that the goitrous disease is not a series of separate conditions, but a process the gradual progression of which one can foretell with as much accuracy as one anticipates the various stages of many other diseases, for example typhoid fever and syphilis.

I have presented this point of view in a measure in several previous papers, and it is my purpose now to treat the subject with greater attention to detail amplified by suitable illustrations which emphasize the various stages. This presentation is based on an intensive study of 1,000 cases in which the specimen, the slide and the case history were constantly at hand. The final results have been checked up as far as possible by a constant contact with the patients after operation until the present writing. This prolonged contact with the patient is necessary for in this way only is it possible to secure an accurate opinion as to what effect the goiter has had on the life of the patient. In my early practice I observed many goitrous patients who were not treated. This gave me a background with which to compare the life history of patients after modern treatment by operation.



Casual observation distinguishes two great classes of goiters. One class is the colloid goiter which, as the name indicates, is characterized by an excessive collection of colloid in the acini with the subsequent development of accessory (possibly compensating) acini often associated with a long line of various types of degeneration. In early life, this type appears as a more or less uniform enlargement that does not cause any considerable disturbance. Appearing in early life, it is called an "adolescent" goiter, there is no other excuse for the name. In maturity this gland becomes irregularly bossiated by the more rapid growth of certain areas. The development continues by successive remissions and exacerbations. After the increased growth is associated with pregnancy or some other periodic disturbance. In this connection it is interesting to note, the comparative rarity of this type in the male. When this bossiated state is reached, the term adenoma has been applied. This is most unfortunate, for in no sense is the term "oma" applicable. The development does not begin at one point and extend from this as tumors do, but all parts of the gland take part simultaneously in the process. The disturbance is in no wise tumorous, but always functional, and the nature and degree of the functional disturbance can be read in the anatomic structure of the gland.

In the other elemental type, there is marked constitutional disturbance associated with marked activity of the gland. The characteristic clinical features are marked nervousness, loss of weight and a greater or less degree of metabolic disturbance. The goiters are then called toxic, a descriptive but noncommittal cognomen. If the patient was known to have a goiter previous to the onset of the symptoms, the term toxic adenoma is applied. If it is not known whether the patient previously had a goiter or not, the term exophthalmic goiter (Grave's disease), is applied because Graves was about the third man, and the first Anglo-Saxon, to describe the disease.

This toxic state is associated with cellular proliferation in the gland with or without actual papillary formation. It is a mistake to assume that the whole gland is made up of this type of structure. As a matter of fact, physicians who have published such pictures in many instances have been obliged to search their slides to find such areas. In doing this, the reader has been unintentionally misled. The larger part of the slide usually is made up of far less active cellular proliferation. True, in a few the larger part of the gland is made up of active gland proliferations with papillabearing areas, but these are rare. In the great majority, a part of the gland is made up of old colloid acini associated with the formation of new acini, with a greater or less number showing active cellular development resulting in papillation. Such colloid-containing acini are now said to be "lugolized."

The cause of the glandular increase is not known. Whether it is developed as a primary process in normal glands or whether the cells are spurred to activity by previous changes in the colloid or merely associated with them is not known. There is evidence of a previous change in the vast majority of cases. In some instances however when the entire gland is involved in diffuse proliferation, its origin in a previously normal gland cannot be disproved.

When a large number of exophthalmic goiters are studied, one finds only a narrow dividing line between the so-called toxic adenomas and exophthalmic goiter. In most cases, if one studies the life history of the patient carefully, the toxic type is an acute exacerbation of a chronic state rather than a new or distinct process. Instead of separating these goiters from old colloids, clarity is achieved by considering them as a variation or continuation of the process. Hence, all goiters may well be considered as stages and variations of a single thyroid disease.

Many cases of exophthalmic goiter of sudden development appear in patients presumably free from goiter. Much confusion has arisen because the patient's word is taken as to the date of the appearance of a goiter. When a patient has a cancer of the breast the size of a walnut and declares that the tumor developed from a bump from a broom-handle ten days previous, physicians are not misled but when a patient says that his goiter first began to develop a few weeks or months ago, the statement is accepted. Yet on examining the gland in the laboratory, old acini, newly developed acini and vascular and other tissue changes are found that must have required years to form. Of course many patients with obvious goiters never knew that they were so afflicted. The patient's statement, as to the duration of a goiter is therefore wholly valueless and must not be accepted. A careful microscopic study of the gland, on the other hand, often gives accurate evidence. A superficial study is not sufficient. The changes in the acini and connective tissue must be studied by specific stains, histochemistry must be brought to the aid of topographic pathology.

In conformity with this conception, therefore, the following groups are to be looked on as the various stages in the development of the goitrous disease rather than separate types. They are mentioned in the order of their occurrence.

#### COLLOID STAGE (ADOLESCENT GOITER)

Adolescent goiter, as the name implies is the goiter of early life. It is characterized by relatively large elastic often soft goiters usually symmetrical in form. Generally they do not markedly disturb the patient but the more I study patients with these early goiters the more I am in doubt as to whether or not they are ever symptomatic. The patient exhibits evidence of nervous hyperactivity and generally a path-

rate that is somewhat augmented. Even from the earliest beginning, one should be reserved in calling goiters innocent.

Though these goiters feel uniform on palpation, a section of them shows a division into lobules (fig 1). This is, of course, only an exaggeration of the divisions in the normal gland.

Histologically, these glands show large acini filled with a homogeneous acidophilic colloid (fig 2). Even in this early stage, there is usually evidence of new gland formation in the interstitial cells and in the walls of the acini. A goiter made up wholly of large acini without any cellular activity is rare, in the 1,000 glands on which this study is

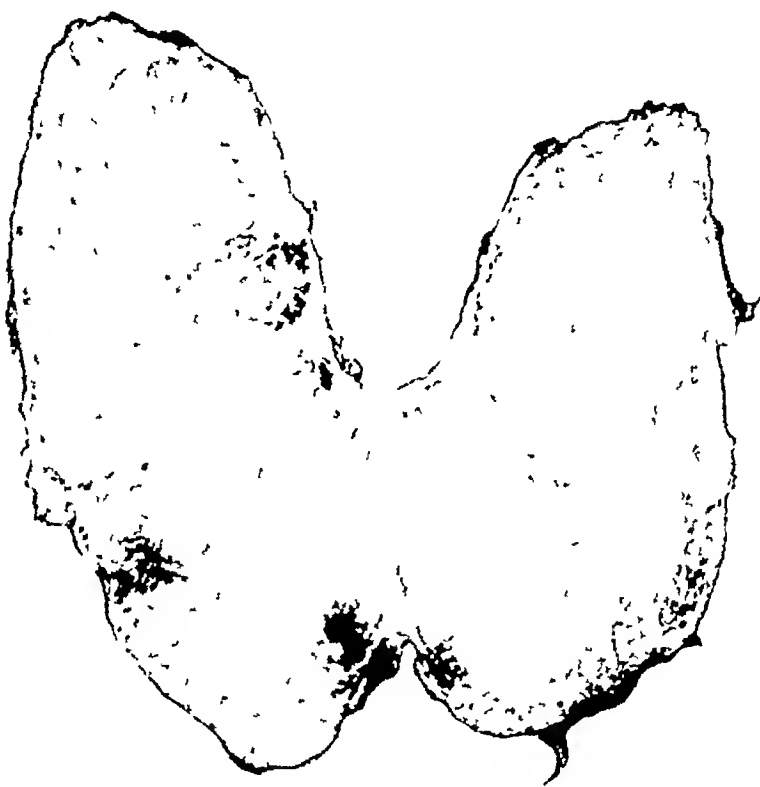


Fig 1—Simple colloid goiter from a boy, aged 14. The division into distinct areas by the fibrous septums is apparent.

based there is not one example of this type. It is true that areas are found which are so large that a photomicrograph may be made of them, but when the whole slide is examined, or slides from various areas, cellular activity will be found in some parts of the gland (fig 3).

Some writers, notably foreign authors, have confused these areas of acinal development with fetal adenomas, to which, of course, they do not bear any resemblance. The fetal adenomas are definitely encapsulated, and the acini are small, the cells are compact, and there is no colloid. These are true tumors, and, though often associated with goiter, are not an integral part of it, but have a life history of their own. Some writers have confused these tumors with the lobulations seen in any

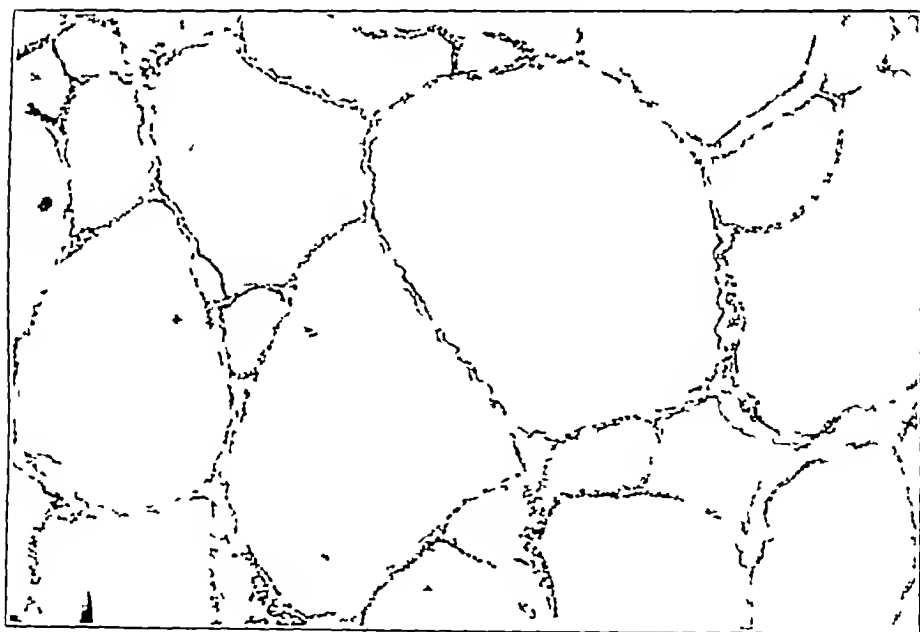


Fig 2—Slide from the gland in figure 1. There is little or no evidence of proliferation of the gland

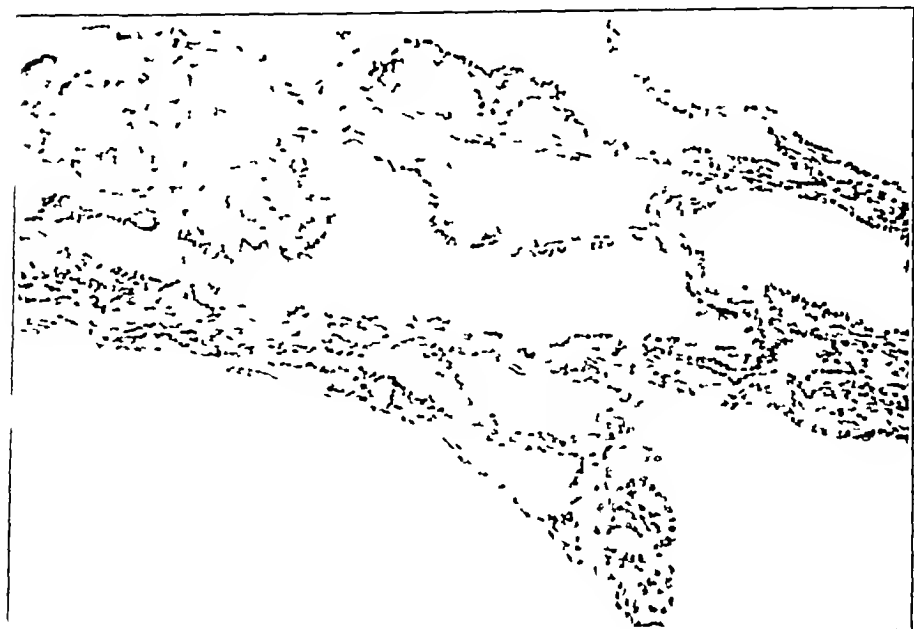


Fig 3—Evidence of gland increase. The photomicrograph is made from a section of a large goiter in a girl, aged 16

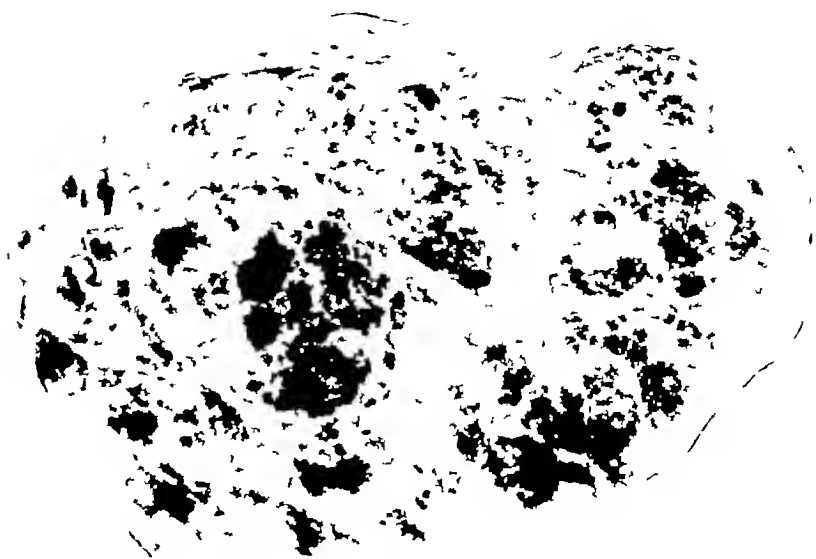


Fig 4—Moderately sized gland showing division into distinct areas by the fibrous septums

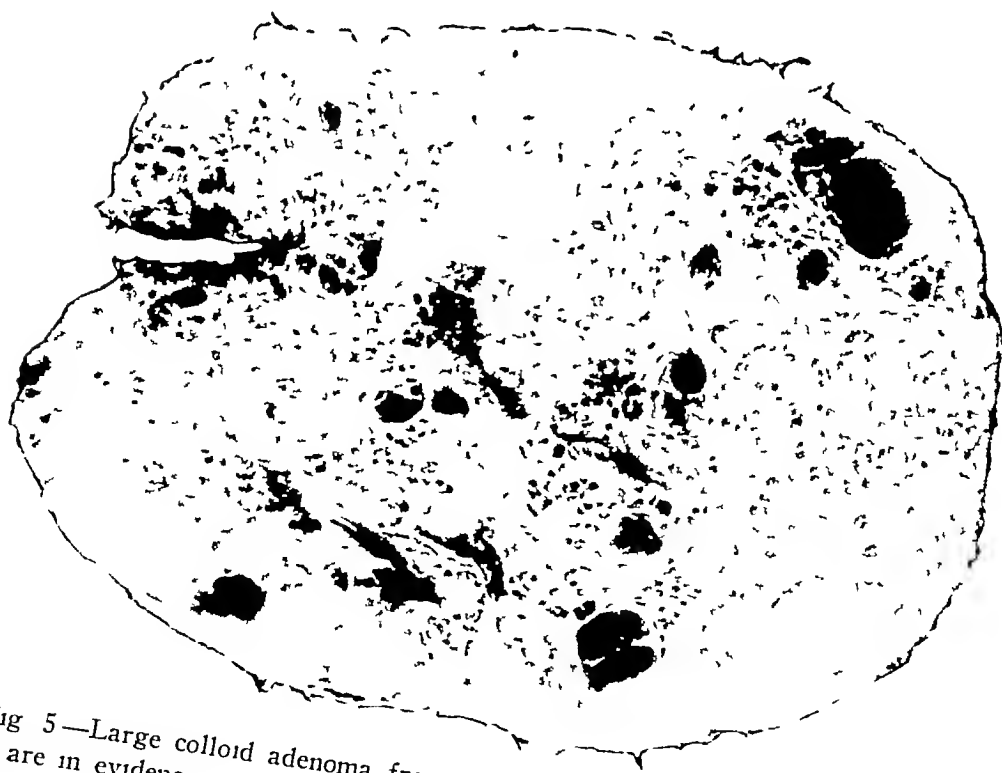


Fig 5—Large colloid adenoma from a girl, aged 20 Numerous good sized cysts are in evidence

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goiter of some age (compare figs 4 and 8). A short sojourn in the laboratory will quickly dispel this delusion.<sup>1</sup>

As the gland develops, encapsulated areas are more apparent (fig 4). These areas are bounded by the natural septums of the gland. In this early stage, small cysts may be present (fig 5), as the disease advances the lobules may become more prominent, the cysts become larger and the fibrous septums more pronounced (fig 6). The entire gland may be made up of such nodules, while the exterior part of it is relatively smooth on palpation. The circumscribed areas appear only on cross-section. It is not yet, in common parlance, an "adenoma."

At this stage, the development of accessory acini may be active (fig 7). Cell masses without lumens appear in the interstitial spaces

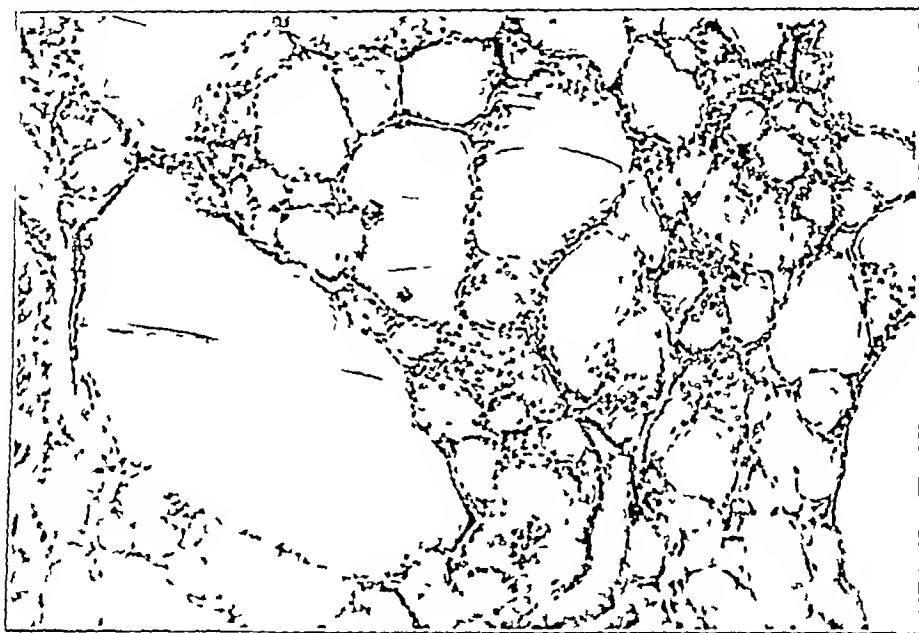


Fig 6—Microscopic section of a goiter removed from a patient, aged 30. The goiter was present fifteen years. The patient has recently shown slight nervousness. Clinically the gland was uniform in outline and elastic to palpation.

In this stage, the patients may or may not complain. Examination will invariably reveal some deviation from the normal, though disturbance of the metabolic rate is seldom one of them.

As a corollary to this stage it is necessary to consider the small firm goiters which Goetsch and I have called interstitial goiters. These are found in girls and young women. The glands are small and symmetrical and usually firm to the touch. It is unfortunate that these have been classed with goiters for they are usually associated with dysmenorrhea and intermenstrual pains. If they were regarded as they should

<sup>1</sup> The structure and life history of the fetal adenomas will be discussed in a subsequent paper.

be, a part of a polyglandular condition, there would be a greater likelihood of properly interpreting the pain in the lower part of the abdomen, and it would help one to understand the nature of the mythical "chronic appendix." Microscopically, these glands show some increase in colloid, but it is usually unchanged. The acinar epithelium is flat. The interstitial cells are prominent, reminding one of the appearance of thyroid glands in children. In these there is little new gland formation.

Sooner or later in goiters of long standing, the nodules, apparent early, become larger, so that the capsule is protruded at certain points and the goiter becomes bossilated on palpation. It is now an adenoma,



Fig 7—Good sized uniform gland from a girl, aged 22. The goiter had been present eight years. The patient declared herself well. The pulse rate varied from 110 to 125, and there had been a loss of 16 pounds (7.3 Kg). She had become nervous and irritable. She was one of the author's office attendants and was under observation a number of years before and after operation. The new gland formation is apparent.

although the histologic structure has not changed. This irregularity of form is brought about by the development of some lobules more rapidly than others (fig 8). It is but an exaggeration of the earlier stage (compare figs 4 and 6). If one has a chance to observe a goiter over many years, one can note the appearance of new bossilations from time to time. In some cases, it seems that the formation of a new bossilation with each pregnancy becomes a milestone in the sands of time.

These bossilations owe their form to the restriction offered by the septums in the fibrous tissue, which characterize the normal gland, being heavier in some regions than in others. On section these bossilations are seen to be made up of many small lobules, each representing a lobule in the normal gland as shown in younger stages.

Histologically, one sees that the increase in size of the lobule, as well as the increase of the colloid content, is dependent on the development of small acini in the interstitial cells or within the walls of the old acini (fig 9). The cells lining the old acini are seen to be flat and endothelial-like, while those of the smaller ones are cuboid, suggesting that these glands are carrying on the function and really constitute a

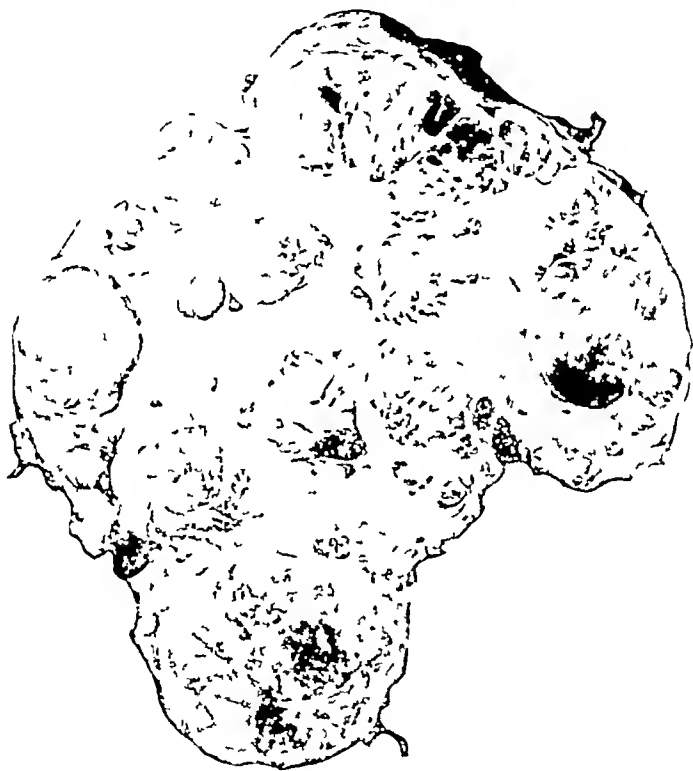


Fig 8—Bossilated goiter removed from woman, aged 35. She had long been nervous and irritable, but otherwise she complained only of pelvic disturbance.

compensatory hypertrophy. The source of the new acini is unquestionably the interstitial cells and probably also the walls of the old acini. It is by this process that the goiter becomes lobulated. The large lobules are usually made up of many smaller ones. These smaller lobules may each undergo changes which are often degenerative, thus giving to the section a mottled appearance.

During this development, the patient is little disturbed. It is the stage of "innocence" and it lasts on an average sixteen years from the time the patient first knew she had a goiter. During this period the patient undergoes the toils and turmoils of raising a family or wishing she had one, and bears the brunt of the give and take known in



domestic bliss, during which she is not always able to tell whether she is sick or just suffering from the joys of life. If her symptoms are studied carefully, periods of nervousness, loss of weight and rapid pulse will be discovered at some time during this stage of development of the goiter. Advanced cardiac disturbance may develop without exciting apprehension. Abundant experience has shown that in the majority of these patients examination will show a disturbed pulse and some disturbance in general health. A patient with a goiter of long standing, whether bossilated or not, is seldom symptom-free. There is little metabolic disturbance at this stage but at intervals loss of weight occurs in many cases.

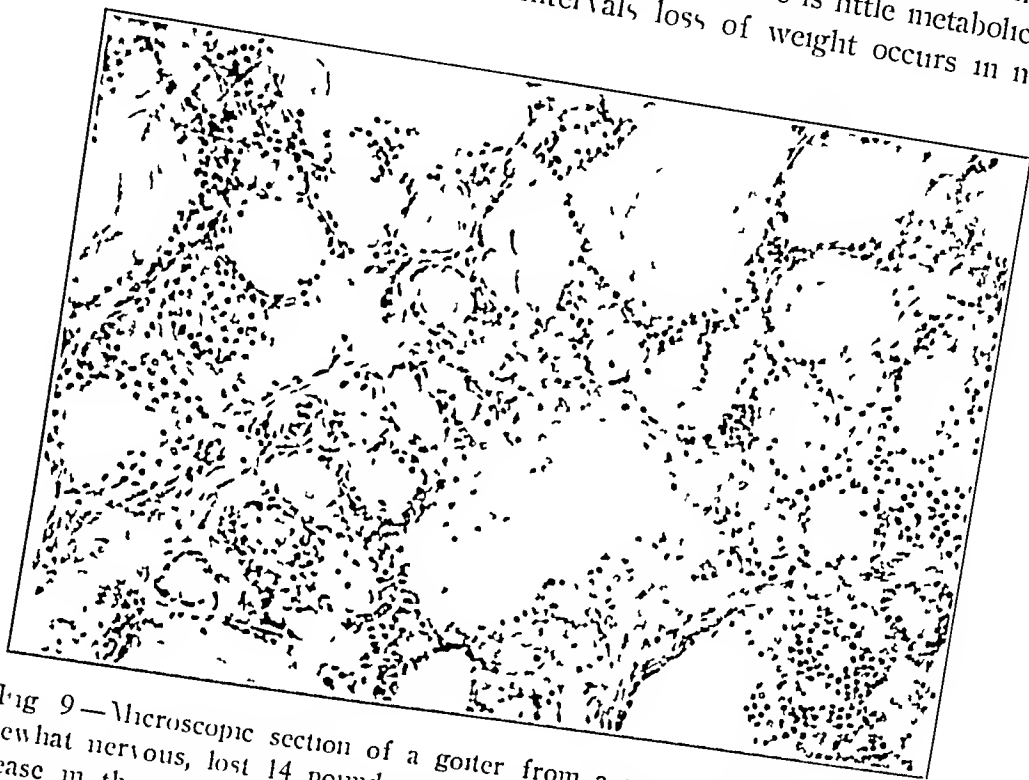


Fig 9—Microscopic section of a goiter from a woman, aged 47. She was somewhat nervous, lost 14 pounds, and had a pulse rate of 125. There is an increase in the small acini similar to that shown in figure 7, but more pronounced. She did not complain of the symptoms of toxic goiter. The foregoing data were obtained in routine examination.

#### CHRONIC TOXIC STAGE (TOXIC ADENOMA)

The chronic toxic adenomas must be distinguished from the acute toxic type, true exophthalmic goiter, which develops on long existing goiters. The toxic symptoms of the chronic stage develop insidiously requiring many years before the patient or her physician is aware that the goiter is the cause of the disturbance of her well-being. Sooner or later, the patient is compelled to recognize definite disturbance. When this stage is reached, there may not be a notable change in the size or outline of the gland or in its consistency, although patients sometimes say that the glands have become larger recently. As a rule, their complaints are not of any physical change in the gland but of

general disturbance. They become nervous, lose weight become sleepless and have a rapid pulse. It is interesting to note that many patients take cognizance of their goiters when they learn that some friend has been cured of an innocent goiter or has died from the effects of one. Innocent goiters seem to be something like practical politics, a person suddenly awakens to the fact that he has been unconsciously suffering for a long time.

Since the operative removal of goiters has become a safe procedure and patients take note much earlier of the smaller ills due to the goiter it has made possible the study of goiters in the intermediate stages. It is only the more ignorant who are operated on late. It is safe to predict

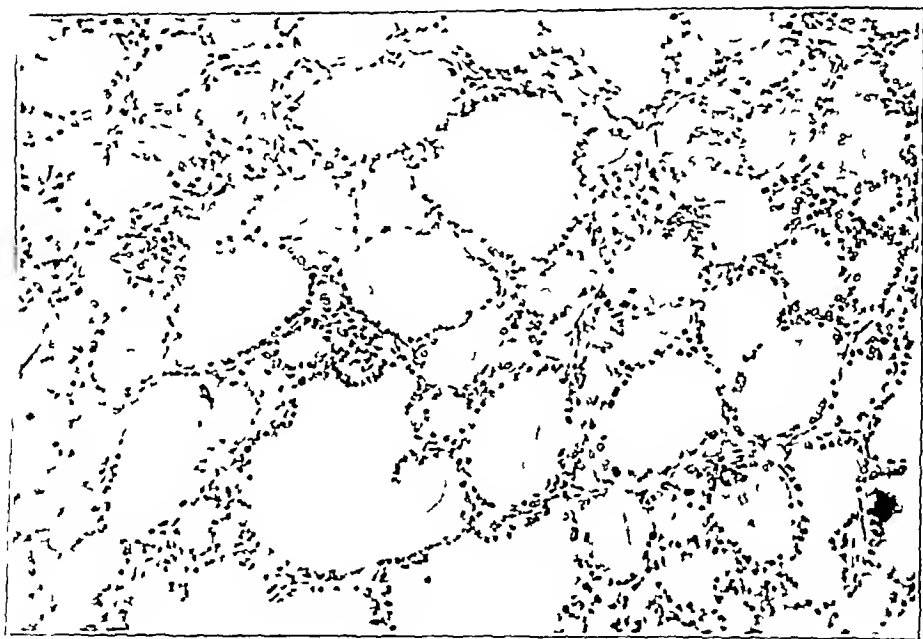


Fig. 10—Microscopic section of a good sized lobulated goiter in a patient aged 42. The pulse rate was 140, basal metabolic rate 44. There was a moderate loss of weight. The cells lining the acini are cuboid and there are many newly formed acini.

that subsequent statistics will show that the interval between the discovery of the enlarged gland and the time of admitted disturbance will be much less than sixteen years.

On section, the picture of toxic adenoma differs from that of the innocent stage of the goiter only in the greater vascularity. The lobulations may be less distinct because the connective tissue undergoes the same regression that it does in highly inflamed tissues that is it is less acidophilic. This results in friability of the gland in every operation. Often when the capsule is torn the gland substance goes out and has the appearance of exuberant granulation tissue. Histologically in the majority of goiters there is cellular activity either in the newly formed acini or in the epithelial lining of the

old acini, generally in both. The cells of the acini are cuboid, seldom columnar (fig 10), and many new acini are in evidence. Various areas of the gland nearly always still show the structure of the old colloid stages, often with extensive degenerative changes, the cellular increase is marked only in certain areas (fig 11). The goiter now has become a toxic adenoma, according to the generally accepted terminology.

In a few of these goiters there is little evidence of cellular activity, but everywhere there is a predominance of degeneration (fig 12). The cells are globular and show a disposition to loosen from the basement membrane, this is notable particularly in those cases in which the patient is not operated on and soon dies. It is difficult to say what part degenerative processes play in the less active cases. It seems to me that too

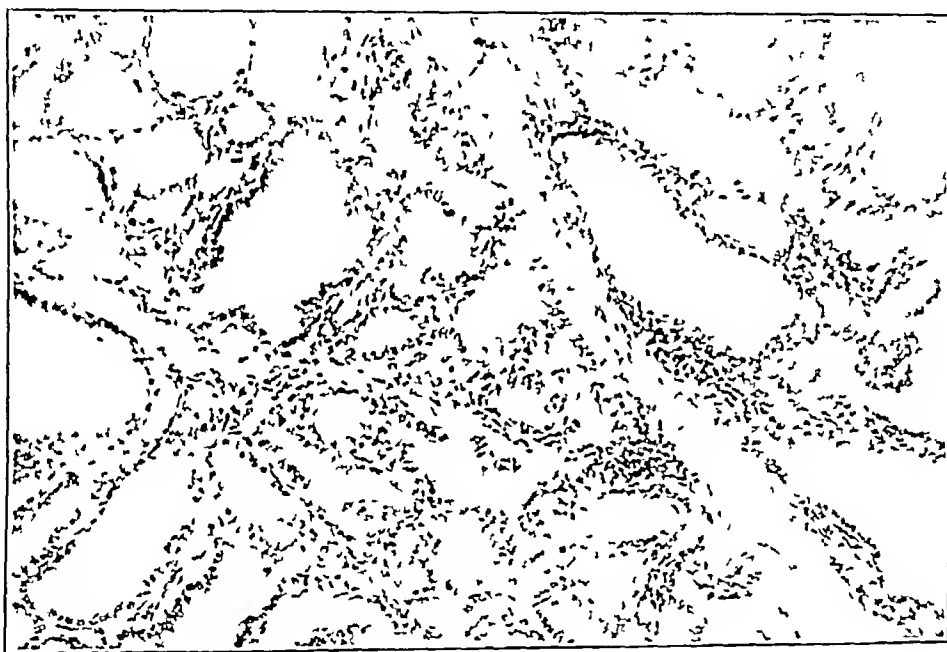


Fig 11—Microscopic section of a goiter from a patient, aged 41, with a clinical history similar to that in the preceding case. The loss in weight was 25 pounds (11.3 Kg). The pulse rate was from 130 to 140.

much attention has been paid to the epithelial changes and too little to the colloid. The epithelial proliferation in these old goiters reminds one of experimental epitheliomas which develop when the acidophilic character of the adjacent connective tissue is reduced by the injection of certain dyes. It is possible that the colloid changes first occur and that the epithelium develops in consequence; there is much evidence to this effect, which every pathologist with an eye trained in histochemistry can verify.

#### ACUTE TOXIC STAGE

In order to trace the relationship of the acutely toxic goiter to the colloid or adenomatous goiter it is best to study first the old colloid goiters which are slowly becoming toxic. The moderate gland prolifera-

tion is at once apparent. In the acutely toxic adenomas, that is those in which an exophthalmic goiter is implanted on an old colloid, this cellular proliferation is seen to be much exaggerated. Old colloid acini may be entirely filled with newly formed cells in some areas while in other areas the old colloid state remains. In the rapidly developing exophthalmic goiters occurring in thyroids not previously known to be goitrous the transition may be more confusing yet in nearly all such cases some areas are found presenting unmistakable evidence of a previously existing colloid change.

At the outset we are confronted by the following well established facts. Exophthalmic goiter is more common in younger persons, the toxicity develops more rapidly, and they have a more pronounced cellular

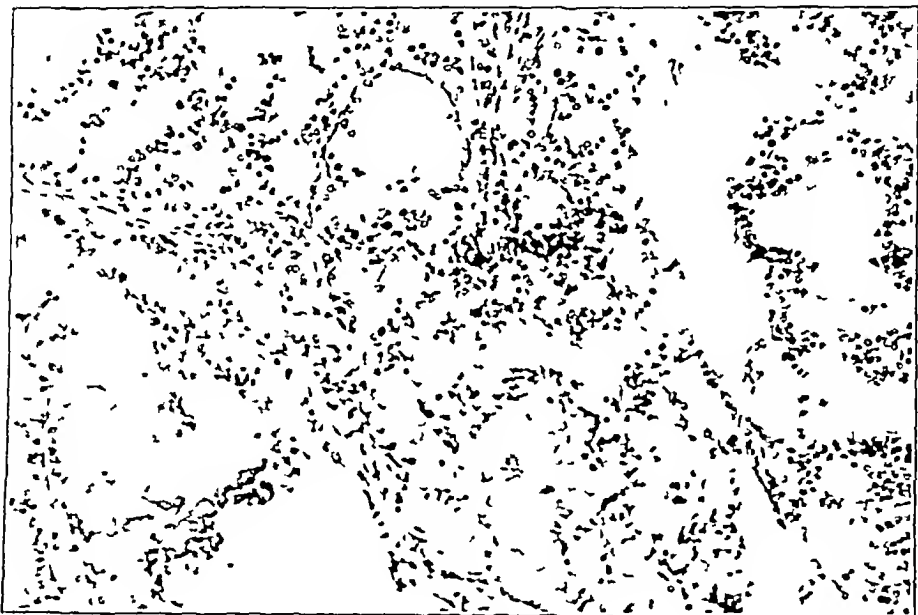


Fig. 12—Microscopic section of a goiter showing marked cellular increase but many of the cells have become loosened from the basement membrane. The patient, a man, aged 48, had had repeated attacks of nervous breakdown with loss of weight.

development. They develop in persons unconscious of having previously had a goiter and they tend more to a spontaneous remission. On the other hand, it is equally well known that they may develop on long existing colloid goiters. When patients present themselves to the physician they say that the goiters are of short duration but on examination of the gland the condition is shown to be of long standing. Many of the patients have not discovered the goiter. There is a gradation between the mild and the severer forms. A patient with a goiter of moderate toxicity commonly refuses operation but after a time she returns to the physician in an extremely toxic condition perhaps with eye signs. Since patients

now present themselves earlier, those with eye signs are becoming rarer. Operation is performed before there has been time for the eye signs to develop.

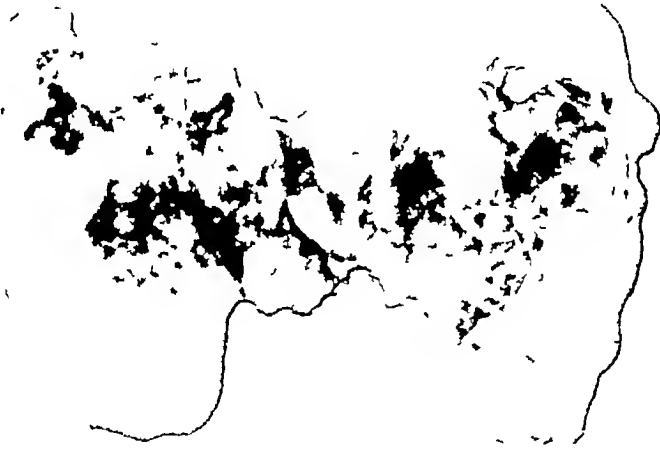
It was formerly the habit to describe dramatic beginnings to exophthalmic goiter. I confess with humiliation that for more than twenty years when patients related to me that their goiters dated but a few months back I accepted that date as the basis of my calculations. Perhaps they dated their troubles from the occurrence of some great emotional disturbance. No one, I dare say, who has suffered a great grief will have escaped the sensation of impending suffocation. Nothing obviously is better calculated to lead to the discovery of the presence of a preexisting goiter. It was only after an accumulation of hundreds of specimens which presented unmistakable microscopic evidence that the goiters were of long standing that it occurred to me that something could be gained by securing a careful history covering the period antedating the time of the alleged origin of the goiter. Since going further back than the suggested date in the history, it is uncommon to find patients with an alleged sudden onset of the condition who do not give evidence of disturbances antedating the time given.

It is not uncommon to see patients who present the symptoms of toxic goiter whose thyroid gland cannot be palpated even by the trained clinician. If the gland is exposed in these persons, however, it will be found to be enlarged, and will show characteristic histologic changes. Therefore, the history of the duration of a goiter is of little practical importance.

While a careful history and a study of the gland materially reduces the number of goiters of sudden onset of toxicity, there are some cases in which both means fail to establish a greater age for the goiter. In such cases, a careful search may fail to reveal any area not involved in active proliferation. On the other hand, I have seen the same process develop rapidly in goiters that I knew existed, although the patients did not. It seems to be an open question whether or not the proliferation characterizing exophthalmic goiter can develop on a previously normal thyroid gland.

Ignoring questions of history and considering only the clinical symptoms and specimens in hand, one finds that this type of goiter is often less lobulated, and that the gland may seem to be uniform in outline. On section, these glands are often gray, and when cut they have a firm feel resembling the sensation experienced when carcinomas are cut. This is due to the reactive changes in the connective tissue, and is not an expression of the degree of cellular development. Generally speaking, the younger the patient the more likely the gland is to be uniform. If these glands are examined carefully, however, while clinically uniform the cut section may show distinct lobulations (fig 13). On the other

Fig. 13—Photograph of the fresh gland in which the lobulations can be well made out. Clinically, the gland was uniform in outline and hard on palpation. The goiter occurred in a patient, aged 22, who had an attack of heart trouble five years ago with some loss of weight. The goiter was first discovered six months ago. The pulse rate was 125, and the loss in weight 29 pounds (13.2 kg.)



The clinical symptoms of this type as contrasted with the more slowly developing toxic adenoma are characterized by greater intensity as well as more rapid onset. The pulse rate is rapid from 110 to 160 the skin is moist, and there is distinct tremor. There is usually a loss

which pulsate the gland which is evident on palpation this is particularly true of those have previously had uniform goiters, there may be an increase in size of more firm, and it may become more sensitive to pressure. In those who of a recent enlargement. The chief change is that the gland becomes great change in the topography of the gland. There may be a history. When the old bossiated goiters become "basedowified" there is not a degeneration

bossiated glands of considerable age often with extensive secondary hand, young girls not previously aware that they had goiters show

forming new glands in the interstitial cells and in the walls of old acini (fig 14), as well as by the papillary projection of cells into the lumen of the acini (fig 15). Areas are found in which there are large acini which contain some vacuolated colloid, while the remainder is filled with papillated excrescences of columnar epithelium. This is particularly true of the glands of children. The cells may be cuboid or cylindric, in the active cases, the latter predominate.

In small glands, the greater part may be made up of such active proliferating cells. In those developing an old colloid, only certain areas are so affected. As many of the acutely toxic glands are found in early life, these glands are usually small, and there is not much evi-

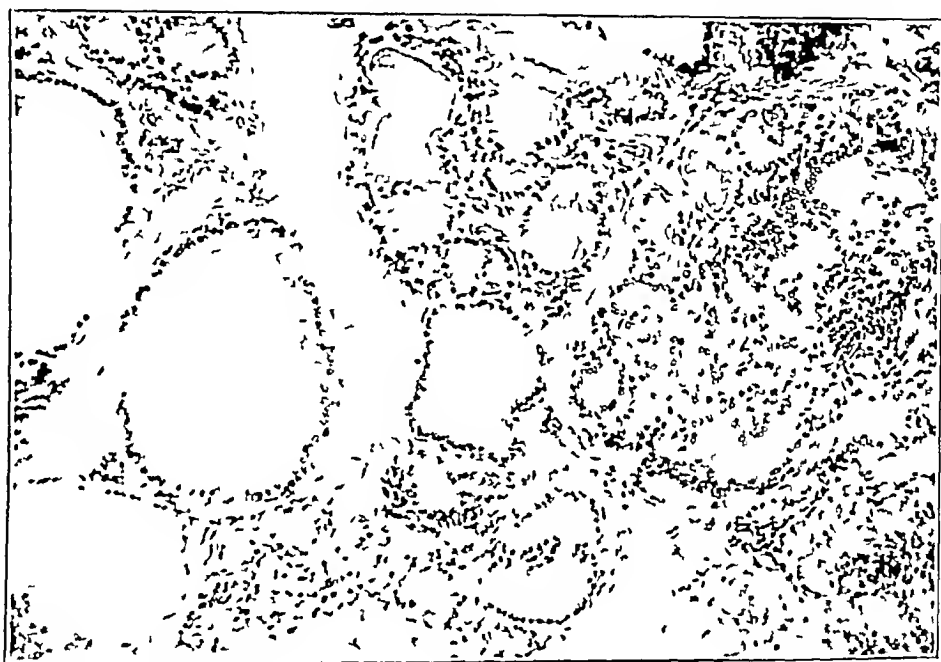


Fig 14—Microscopic section of a bilateral, soft goiter. The patient had lost 50 pounds (22.7 Kg.), had a pulse rate of 104 and showed marked loss of strength. The goiter had not been discovered before he entered the hospital. The cells lining the acini are cuboid and columnar in some areas, some masses of interstitial cells without lumina are seen.

dence of old colloid change. It takes many years to produce an old, lobulated colloid goiter. If one keeps in mind the age of the patient and the size of the gland, the histologic picture may be predicted. In the older glands, whether the patient is old or not, only areas here and there may show the active cellular proliferation, and papillated areas may be rare. Bossilated glands do not show masses of gland proliferation no matter what the clinical symptoms may be. In some cases of old goiters, several blocks of tissue must be cut before a characteristic area is found. It is certain, however, that if the symptoms are those of toxic goiter, areas of gland proliferation will be found, and if the symptoms are those

of exophthalmic goiter, that is, if eye signs are present, papillated areas will be found. When these facts are kept in mind the relation of the primary toxic and the "basedowified" adenoma is apparent. In rare instances there is evidence of gland degeneration without cell proliferation (fig. 16). These cases make me wonder whether or not too much emphasis is placed on cell proliferation and too little on degeneration in the interpretation of the very fondroyant cases. Evidence of degeneration is most apt to be seen in the rapidly fatal cases. In some of these, the size of the gland rapidly decreases as death approaches. It is as though the colloid had suddenly become absorbable and had overwhelmed the patient.

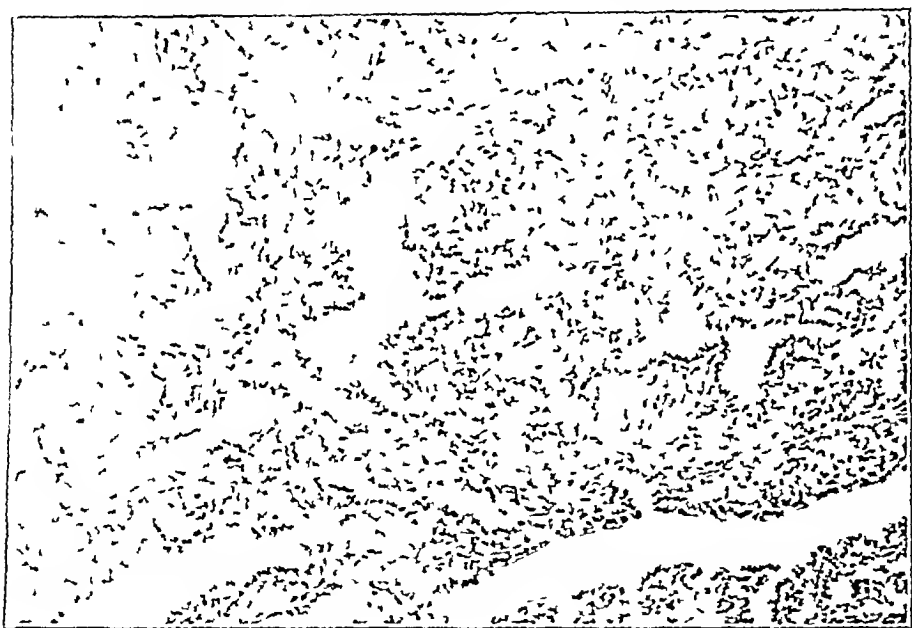


Fig. 15—Microscopic section of a goiter showing marked cellular proliferation with papillation into the acini which are free from colloid.

#### COMMENT

It is only by viewing the disease of the thyroid gland as a continuous process that the therapeutic indications become clear. Anatomic changes cannot be relieved by internal medication, it is only in the early stages that a complete cure by medication is possible. It is the age of the goiter that counts not the age of the patient. In the earlier stages evidences of disturbances are evident and perception of what they are eventually lead to saves one from the error of considering them as until irreparable damage has been done. Every complaint that a patient may have should not be ascribed to the presence of a goiter. Papillation of the neck should be the last act in the physical examination. If patients should not be the first to discover that the goiter is there, then



So far as their tendency to destroy life is concerned, goiters, particularly the innocent colloids, should be compared with malignant tumors. It is as important to recognize an impending danger in its incipency in goiter as it is to recognize this in cancer. The fact that the development of goiters may require generations whereas cancers require years does not alter the gravity of the problem. Only surgeons are in a position to obtain the material which makes possible a correct understanding of thyroid disease, and consequently patients with goiter should be under the eye of the surgeon. Medical treatment during all except the early stages of goiter is as deadly as medical treatment for cancer. The analogy is not apparent, because the goitrous process is more insidious and kills without revealing the error of

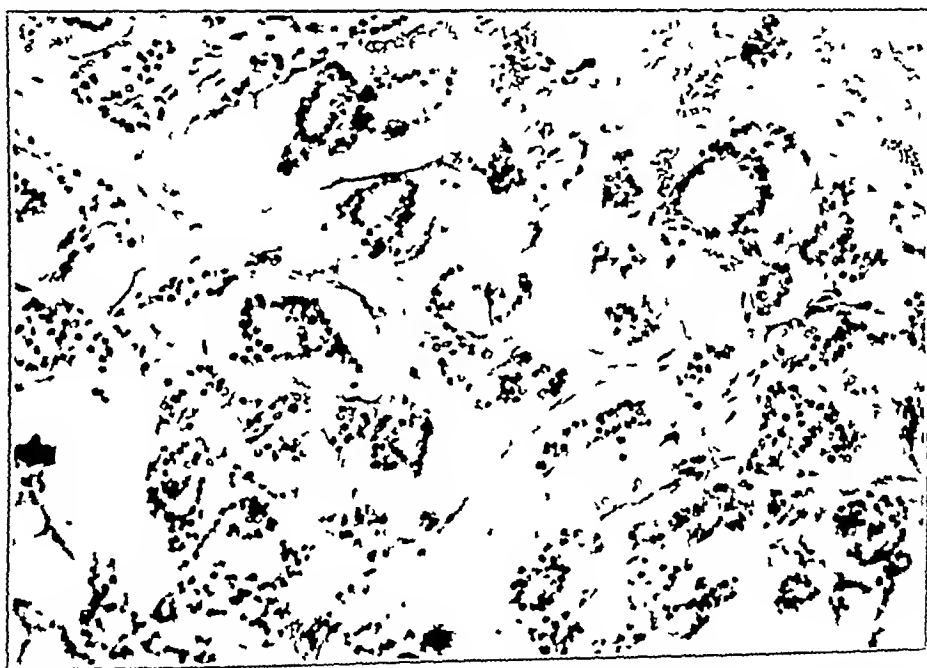


Fig 16—Microscopic section of a toxic goiter, showing a marked cellular increase. The cells are loosened from the basement membrane.

madequate treatment. Patients living in this region who thirty years ago had innocent goiters have all died of cardiac failure.

#### SUMMARY

- 1 Colloid goiters early show evidence of new gland formation.
- 2 The formation of lobules within the gland begins with the first proliferation of cells.
- 3 Bossilated goiters are not different in structure than those uniform in outline, except that the process is more advanced.
- 4 The toxic stage is always associated with increased proliferation of the gland.
- 5 The so-called exophthalmic goiter differs from the so-called toxic adenoma in degree and in rapidity of development but not in kind.

# RELATION OF HYPERTHYROIDISM TO BENIGN TUMORS OF THE THYROID GLAND\*

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AND

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The pathologic significance of benign nodules or tumors in the thyroid body and their relation to states of hyperactivity of the gland are subjects concerning which there are profound differences of opinion and widespread confusion. The view most generally accepted up to the present time has been that all the tumefactions or nodules in cases of nodular goiter are adenomas, in the sense of true benign neoplasms, and that any anatomic or functional disturbances occurring in these patients are due to the activity and growth of the tumors. It is our purpose in this paper to present a brief analysis of 109 consecutive cases of nodular goiter with hyperthyroidism in which the patients were operated on during the last year, together with a review of 910 cases of hyperthyroidism and as a result of this study to present a conception of the pathologic and clinical significance of benign tumors of the thyroid gland which differs markedly and fundamentally from that held at the present time.

In a recent study,<sup>1</sup> it was demonstrated that concomitantly with an artificial or iodine remission in patients with euthyroid hyperthyroidism or exophthalmic goiter a transformation from an extreme hypertrophy and hyperplasia to a resting or colloid state more nearly approximating the microscopic appearance of a normal gland occurred in the microscopic structure of the thyroid. This transformation was termed an involution of the gland and a terminology used to describe analogous regressive changes in the breast, ovary and uterus. Sections from the thyroid of seven patients were examined before, during and after the administration of iodine in sufficient dosage to produce an artificial remission so that in this way we were able to make a comparative study of the clinical course of the disease and of the histologic changes within the gland. The thyroid parenchyma which was removed and examined previous to an artificial remission brought about by iodine revealed a marked diffuse hypertrophy and hyperplasia in all instances. The hypertrophy of the thyroid cells was similar in all the cases, but a difference was noted in the type of hyperplasia encountered. In one type of hyperplasia this difference consisted mainly in the presence of

\*From the Thyroid Clinic of the Johns Hopkins Hospital.  
1 Rienhoff W. F.: Involution or Regressive Changes in the Thyroid in Exophthalmic Goiter and Their Relation to Operation. *Arch. Surg.* 13: 351 (Sept.) 1926.

delimited areas or apparent lobules which contained large lacelike acini (fig 1) with papillomatous-like infoldings of the epithelium projecting into the lumen, but despite the increase in the size, the number of acini remained apparently about the same as in the lobule of the normal gland. In the other type, however, there seemed to be an increase in the number of acini. These acini were small, round structures in which little if any infolding of the epithelium was noted (fig 2). They were also regular in size and shape, and resembled somewhat the fetal acinus in structure and appearance. This difference in the hyperplasia of the parenchyma was also noted in 557 consecutive cases of exophthal-

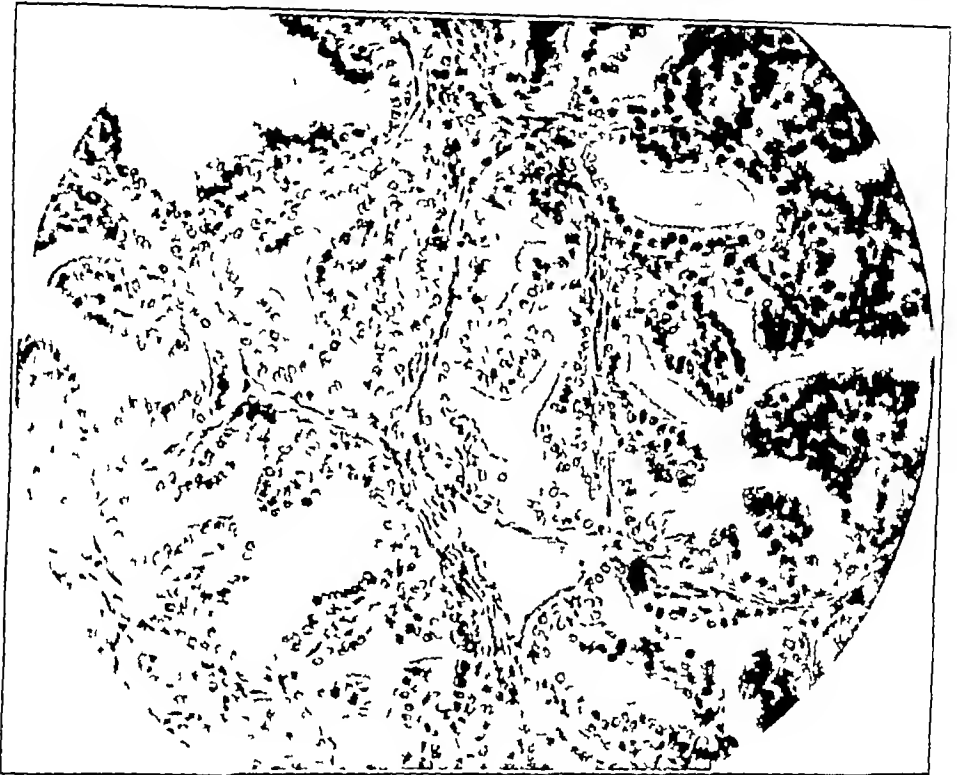


Fig 1—Typical microscopic picture of hypertrophy and hyperplasia of thyroid gland from case of exophthalmic goiter removed before administration of iodine. Note papillomatous infolding of epithelium into lumen of acini. Reduced from a magnification of  $\times 176$ .

mic goiter in the Johns Hopkins Hospital. In the majority of cases, there were lobules representative of both types of hyperplasia, but in some, one type predominated throughout the gland as a whole. The large acini with papillomatous infolding were the type most frequently encountered. Mention is made of these distinct types in some detail because the process of involution seemed to differ to some extent, depending on the type of hyperplasia in which the process had its beginning. The remaining characteristic features of hypertrophy and hyperplasia of the thyroid parenchyma are too well known to require repetition here.

In the seven controlled cases already referred to the regressing state of involution was characterized by (1) a marked increase in the amount of colloid in its viscosity and in its avidity for stains (2) an increase in the size and regularity of the acini (3) a decrease in the height and size of the epithelial cells, (4) a decrease in the cystoph-



Fig 2—Histologic appearance of thyroid parenchyma in case of cystoph-  
goster. Note hypertrophy same as in figure 1 but there is a very small  
small acini without papillomatous infolding of epithelium. (H&E stain,  
magnification of  $\times 176$ )

mic constituents of the epithelial cells (5) an increase in the amount of  
of the nuclei (6) a decrease in the lymphocytic infiltration (7) a  
decrease in the vascularity of the gland and (8) a proportionate decrease  
in the fibrous connective tissue separating the nodules (9).

(figs 3 and 4) In some instances, the deposition of this fibrous tissue resulted in a veritable sclerosis of the lobule and even of the entire gland. The latter state was thus shown to be less active physiologically as well as histologically than the former one of hypertrophy and hyperplasia. This regression in the hyperplastic gland or involution was usually a diffuse process, which occurred to about the same extent throughout the gland as a whole. The degree of involution observed in the seven controlled cases, which was found also in 200 subsequent cases of exophthalmic goiter that had undergone an artificial remission after iodine, was reckoned as the average or normal degree of involution.

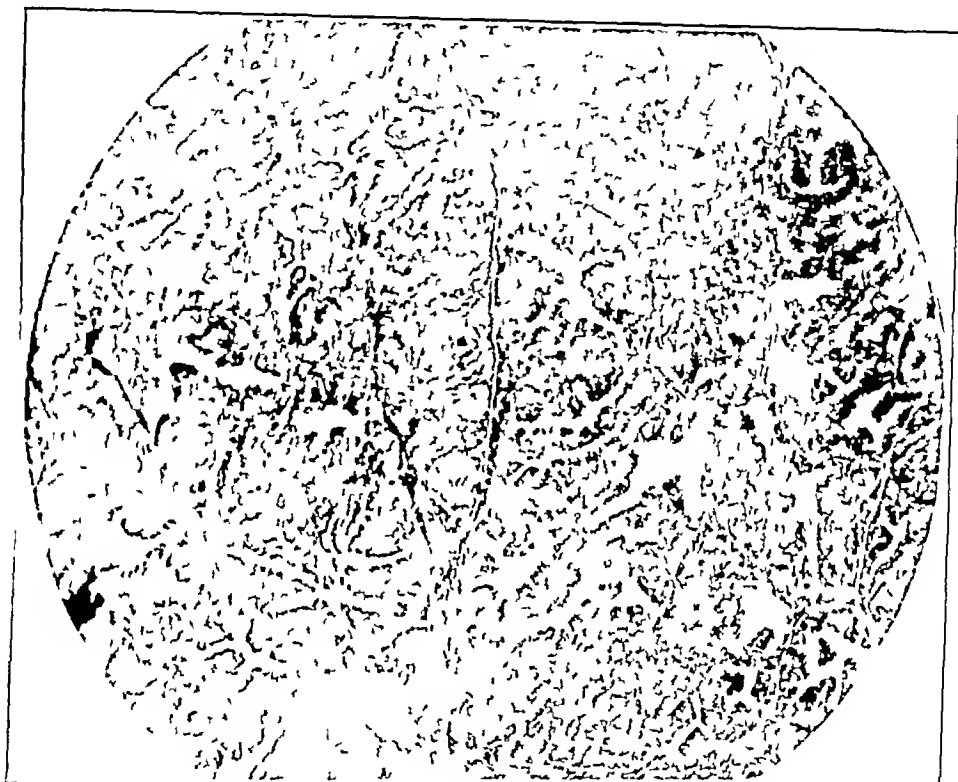


Fig 3—Section of tissue removed from thyroid gland of case of exophthalmic goiter before administration of iodine showing classic microscopic picture of hypertrophy and hyperplasia of the thyroid gland. Reduced from a magnification of  $\times 40$ .

that occurs during such a remission. In some lobules or areas, however, the process of involution was incomplete or absent, hypoinvolution, while in others it had extended beyond the average degree, hyperinvolution. The lobules or areas of hypoinvolution (fig. 5) appeared to be localized and encapsulated areas of hyperplasia which were composed of small, round acini. In and about these areas was an infiltration of small lymphocytes. They were areas in which either the involutional changes affecting the remainder of the gland had been resisted or (as Dr W. G. MacCallum suggested) the disease process was beginning all over again. They

suggested histologically, the so-called diffuse and miliary adenomas of some observers. The areas of hyperinvolution more common and of larger size, were designated as involutional bodies. They could be detected as nodosities on the surface of the thyroid by palpation not only grossly, but also clinically, and when the thyroid as a whole became enlarged, following the deposition of colloid, these nodosities also increased in size. (On microscopic examination not only did they prove to be areas or lobules of the gland which had gone on to more complete involution than the usual degree occurring throughout the thyroid dur-

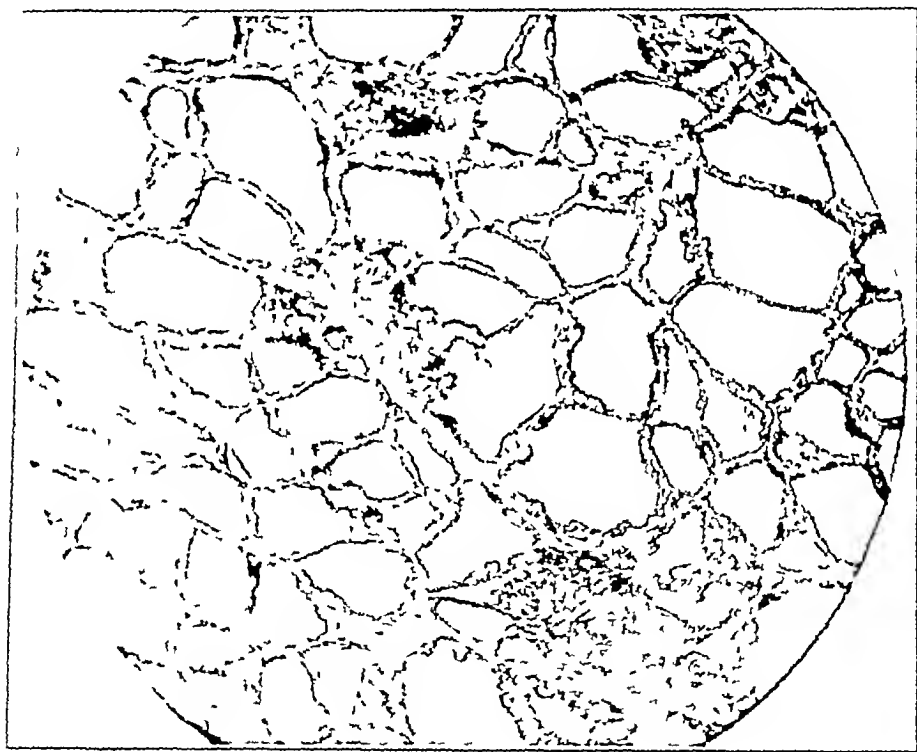


Fig. 4—Section of thyroid from same patient as in figure 3 following the administration of iodine. Note involutional changes in the histologic structure of the gland. This is representative of the average degree of involution occurring in an artificial iodine remission. Reduced from a magnification of  $\times 40$ .

ing a remission, but in some a histologic regression that approximated an actual degeneration of the parenchyma was noted. Histologically these involutional bodies fall into three general groups, (1) those showing a formation of large epithelioid-follicles containing colloid (figs 6 and 7), (2) those showing localized and scattered areas of dilated colloid-containing (miliary) follicles, and (3) those distinguishable from the so-called colloid adenomas (figs 8 and 9) by showing areas or lobules in which the process of involution is carried far beyond the average found throughout the gland, even suppressing the more complete involution of the entire gland.

type mentioned and approaching a state of actual disintegration of the parenchyma (figs 9 and 10) This extreme degree of hyperinvolution was usually limited to one area or lobule, and it was characterized by a breaking up of the acini, especially toward the center Thus, not only did the number of intact acini remaining for the lobule diminish, but those that had resisted the involution were separated by a larger

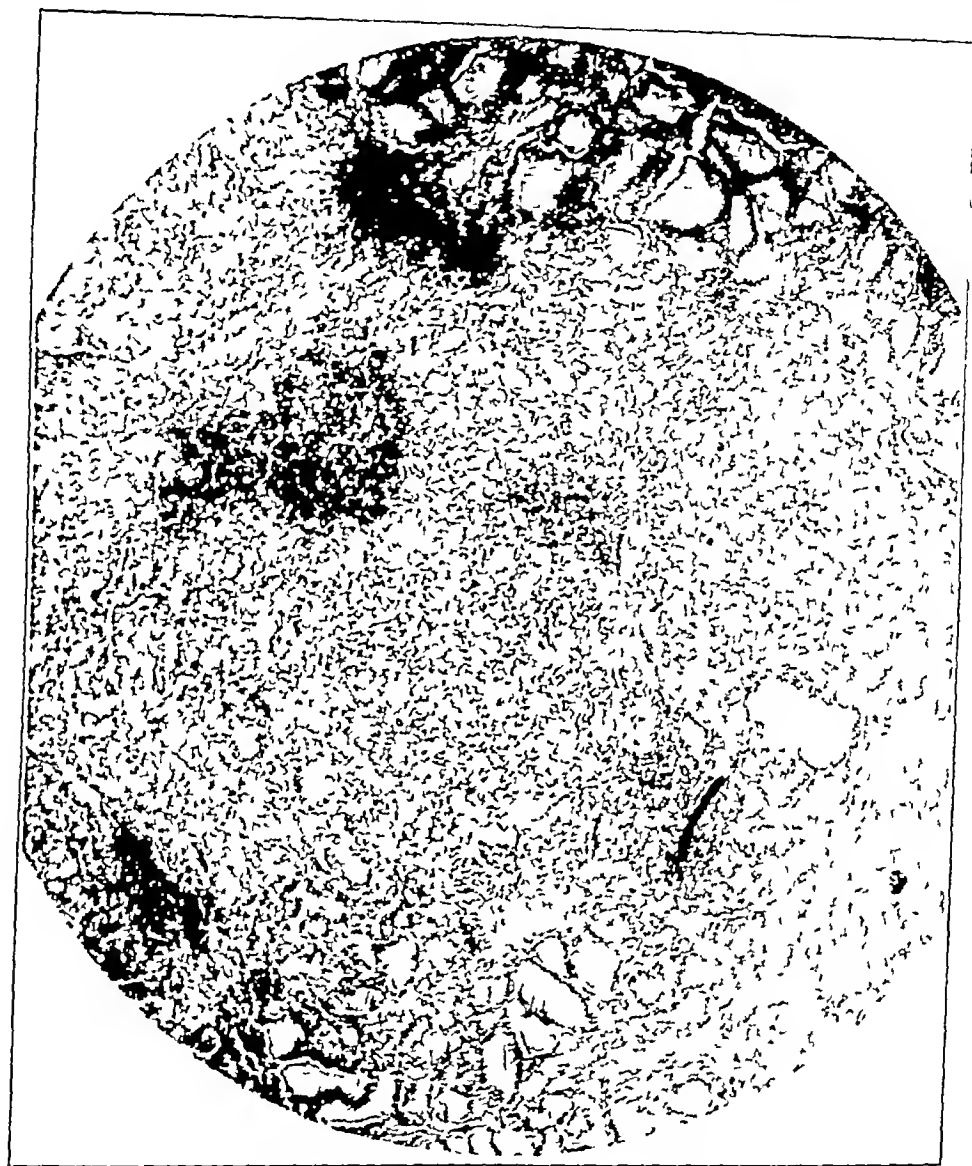


Fig 5—Average degree of involution which occurred throughout the gland as a whole can be seen in margins of photomicrograph In the center, however, can be noted an area containing many small acini or tubule-like follicles of cuboidal epithelial cells the apices of which abut on each other and in which the lumen, if any, is small Three areas of lymphocytic infiltration can be seen, the presence of which would suggest a localized area of histologic hyperactivity The area of persistent hypertrophy and hyperplasia or hypoinvolution seems to be confined to one lobule, the margins of which can be seen in the upper portion of the figure The intralobular stroma is delicate Reduced from a magnification of  $\times 40$

This increase in the stroma resulted partly from an actual increase in the fibrous connective tissue and partly from a premeation of this connective tissue by the colloid which had escaped from the disintegrated acini. Desquamated epithelial cells could be found singly and in clusters throughout this stroma and here and there nuclei which had been extruded from the cells could be seen. The microscopic picture was one of marked histologic regression and degeneration. Here, as elsewhere, in the gland whenever involution had occurred there was an increase in the size of the area due to the excessive deposition of colloid. As a consequence the areas or lobules undergoing hyperinvolution were increased in size and volume to a greater extent than the surrounding parenchyma and this gave rise to a pronounced distortion of the acini of bordering lobules with their associated inter-

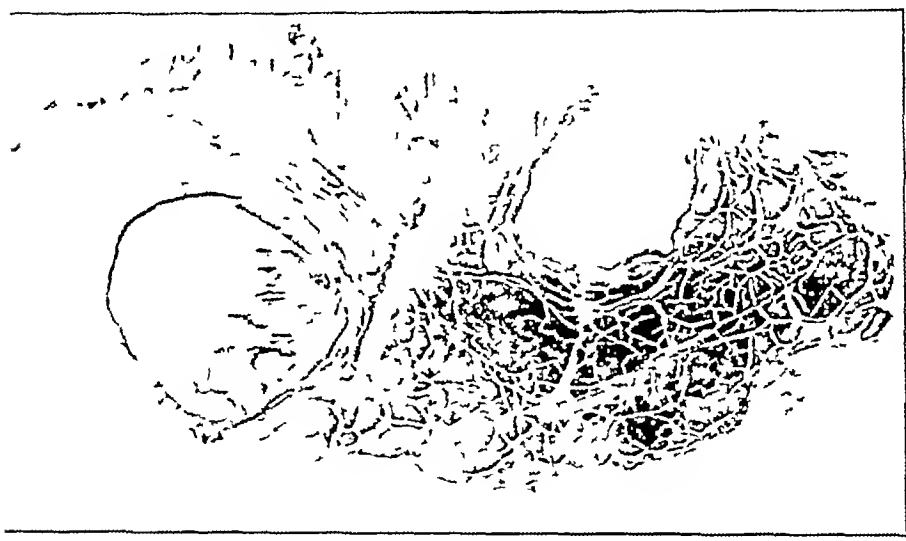


Fig. 6—Section across entire lobe of thyroid gland involution of the patient with iodine and the occurrence of involution. The thyroid gland diffusely enlarged and smooth became nodular after treatment with iodine. Many large colloid cysts and localized areas of dilated follicles appeared some of which could be rich clinically. No compression of the acini about the large cysts as well as compression of the acini. A fairly definite cystoma of this nature. These demonstrate one type of hyperplasia reduced from a magnification of 2700.

lobular and intralobular septums (figs. 7 and 8). This hyperplasia of the stroma produced an apparent compression of the acini. Hyperinvolution became more sharply defined in the flattened acini and strands of fibrous stroma of the stroma. The numerous parenchyma resisted to the origin and growth of this hyperplasia of the capsule. This hyperplasia of the capsule suggested strongly the possibility of a cystoma. The thyroid gland involution suggested strongly the possibility of a cystoma.





Fig 7—Area of hyperinvolution in the form of a large colloid cyst which developed in the gland during involution. Many of these cysts were present in this case. The average amount of involution occurring throughout the gland as a whole can be seen about the periphery of a figure. The beginning formation of a capsule about this colloid cyst can be seen in the compressed interlobular as well as in the intralobular stroma and the compressed peripherally situated small acini. The epithelial cells lining the cysts are much flattened, approximating endothelial cells. All changes point to an extreme involution or regression of the parenchyma. There is no evidence of hyperactivity of the tissue in either growth or function. Reduced from a magnification of  $\times 40$ .

of involutional body seemed to occur more frequently in the thyroid glands in which the parenchyma was composed of the small acinar type of hyperplasia already referred to (fig 2) whereas the glands in which the acini were originally of the large lacchke type containing papillomatous infoldings (fig 1) gave rise to areas of hyperinvolution made up largely of cysts and encapsulated areas of dilated colloid-containing acini. In the majority of the cases all of the three types of hyperinvolution or involutional bodies were observed although individual cases differed to some extent in the completeness of the artificial trans-

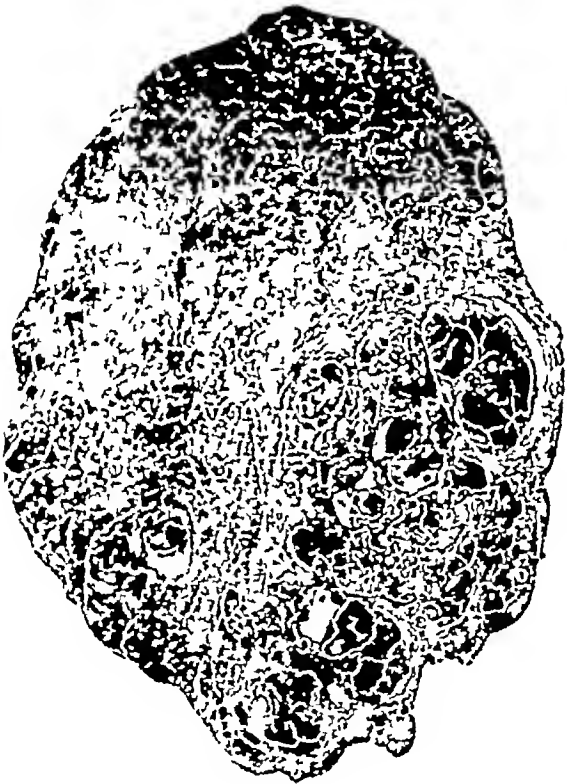


fig 8—Photomicrograph of section across entire pole of thyroid gland after treatment of the patient with iodine. Note areas of hyperinvolution which late macroscopically the so-called colloid adenomas. The thyroid gland and these areas has undergone average amount of involutional changes. Taken from a magnification of X 16

sion and also in the degree of involution. The latter is a reflection of iodine given and the length of its administration being taken into consideration. Just as the reactions and reparative processes are exaggerated and overdone after an injury elsewhere in the body, so the return areas of the hyperplastic thyroid parenchyma to normal in the gland in these lobules goes to a great extent. But it was observed that although these areas return to normal

involutional bodies formed localized palpable tumefactions, in general they maintained the structure of the normal hyperplastic thyroid parenchyma and did not show any such formation of new tissue as is commonly seen in a neoplasm, but rather regression and disintegration. Thus, these bodies differed in the microscopic appearance from a true benign neoplasm which always shows evidence of the formation of new tissue and more or less marked cellular regeneration.

In a further study of fifty cases of exophthalmic goiter in which spontaneous remissions and exacerbations had occurred and in which the thyroid had been partially removed during an exacerbation, it was



Fig 9—Areas of extreme hyperinvolution following the administration of iodine termed in this study as the third type that approximates degeneration, inequality in size of acini, extreme involution of epithelium and pyknotic nuclei, disintegrating acini, with the result that small clumps of epithelium are deposited in the abundant stroma the stroma here is partly made up of colloid which has escaped from the acini due to this disintegration, this type of disintegration is frequently seen in areas of extreme involution. Reduced from a magnification of  $\times 67$ .

found that the gland was always nodular, and that these nodules could be palpated clinically as well as in the gross specimens. In the cases in which accurate and careful histories could be obtained, the information was elicited that the nodules had originally appeared after a nervous attack and had become enlarged after each successive exacerbation of the disease. In these cases gross as well as microscopic examinations

proved that the nodules were identical in all respects with the involutional bodies found after an artificial remission caused by iodine except that the latter were uniformly smaller than the nodules that developed after spontaneous remissions (figs. 11, 12 and 13). This difference in size is readily explicable if it is remembered that the areas of hypertrophy and hyperplasia associated with involution—and that they have been developed in a relatively short space of time in from two to four weeks, whereas the nodules resulting from the spontaneous remissions may be the products of not one but of many disease cycles



Fig. 10—Typical area of extreme hyperinvolution occurring after the cessation of iodine and involution. The histologic appearance in this area is characteristic of the nodules. The stroma is markedly free of edematous in appearance. The acini are small and widely separated. The acini have degenerated and become broken up. The acini are scattered throughout the stroma in small groups. The acini are extremely colloid. The microscopic picture is one of extreme involution of new tissue. Reduced from a magnification of 125.

extending over a period of months or more after the cessation of iodine. Involutional bodies in these cases showed the same histologic appearance that had occurred in general throughout the gland. The nodules of the hyperplasia (figs. 11, 12 and 13). In these cases the nodules were found to be identical with the nodules found after an artificial remission caused by iodine except that the latter were uniformly smaller than the nodules that developed after spontaneous remissions (figs. 11, 12 and 13). This difference in size is readily explicable if it is remembered that the areas of hypertrophy and hyperplasia associated with involution—and that they have been developed in a relatively short space of time in from two to four weeks, whereas the nodules resulting from the spontaneous remissions may be the products of not one but of many disease cycles



Fig 11—Area of hyperinvolution that has occurred in the thyroid gland of patients undergoing spontaneous remissions in which a subsequent exacerbation had occurred when the gland was removed by operation, the histologic alterations observed in these cases following a spontaneous involution will be seen to correspond exactly with the involutional changes following an artificial remission or involution. Reduced from a magnification of  $\times 16$



Fig 12—Area of hyperinvolution that has occurred in the thyroid gland of patients undergoing spontaneous remissions in which a subsequent exacerbation had occurred when the gland was removed by operation, the histologic alterations observed in these cases following a spontaneous involution will be seen to correspond exactly with the involutional changes following an artificial remission or involution. Reduced from a magnification of  $\times 16$

of dilated colloid-containing acini there was a tendency for the epithelium to undergo papillomatous infolding during an exacerbation of the disease (and probably in each exacerbation) followed by a further ballooning out and distention due to the deposition of colloid accompanying the involution associated with a spontaneous remission (Figs 12 and 13). In the lobules or regions of extreme hypervasculation the functioning epithelium was relatively and actually reduced during remission, and there was marked fibrosis toward the center of the lobule (Fig 11). Therefore accompanying an exacerbation in this type of involutional body there was a peripheral zone of marked hypervasculation.

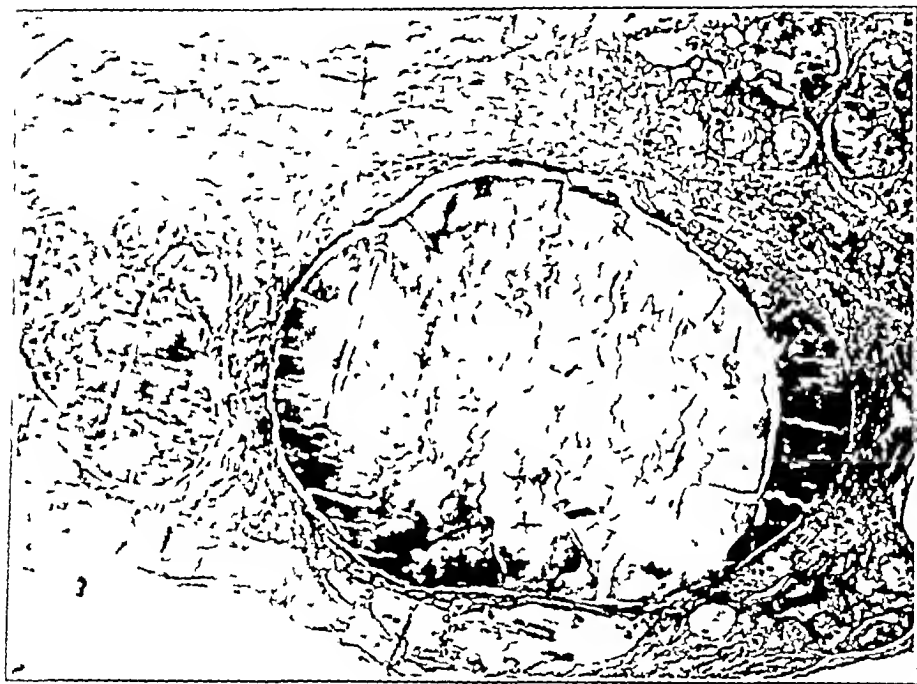


Fig. 13—Area of hyperinvolution that has occurred in the left patients undergoes spontaneous remissions in which a spontaneous reduction occurs when the gland was removed by operation. It has been observed in these cases following spontaneous involution that the gland respond exactly with the involution changes following an involution reduction. Reduced from a malignant condition. It

and hyperplastic stem which become more sparsely distributed by the substitution of fibrous tissue as one appears to be tubular. The peripheral zone of cortical hyaline is associated with the excretions as in the case of the degeneration or degeneration during maturation. The intra-arterial cobord in these areas is the greater the number of capillaries involved in the involuntarily located by the

distinguished from the actual growth of a true neoplasm. Although these areas of hyperinvolution can be detected clinically as tumors, they are not true neoplasms or adenomas, because they have been observed to occur and develop during an artificial involution of the thyroid gland following treatment with iodine as well as after a spontaneous clinical remission. They also present throughout the microscopic characteristics of regression, disintegration or degeneration, and not of regeneration, with increased growth activity or actual increase of new tissue as in a neoplasm. Representing as they do regressive sequelae of a previous hypertrophy and hyperplasia of the parenchyma, the involu-



Fig 14—True benign neoplasm of thyroid gland. Histologic pattern is unlike that of normal or hyperplastic thyroid parenchyma. The epithelial elements are in anastomosing columns. Bizarre-shaped acini are near the periphery. Reduced from a magnification of  $\times 8$ .

tional bodies still maintain the structure of the normal gland parenchyma to a large extent, and, as shown in those cases undergoing spontaneous remissions and exacerbations, they become involved in the generalized hypertrophy and hyperplasia supervening throughout the gland as a whole during a recurrence of the active phase of the disease. A true benign neoplasm (adenoma) does not undergo hypertrophy and hyperplasia in sympathy with the remainder of the gland in which it has grown.

It can, therefore, be concluded that associated with atypical and spontaneous remissions in cases of extreme hyperthyroidism or exophthalmic goiter, nodules or clinically benign tumors are formed during involution of the gland, these are not true neoplasms but they are composed of hyperinvolved and disintegrating parenchyma that has undergone histologic regression

# NODULAR GOITER ASSOCIATED WITH HYPERTHYROIDISM

The striking and rapid changes of the histologic structure in the thyroid gland the production of involutional bodies which occur during

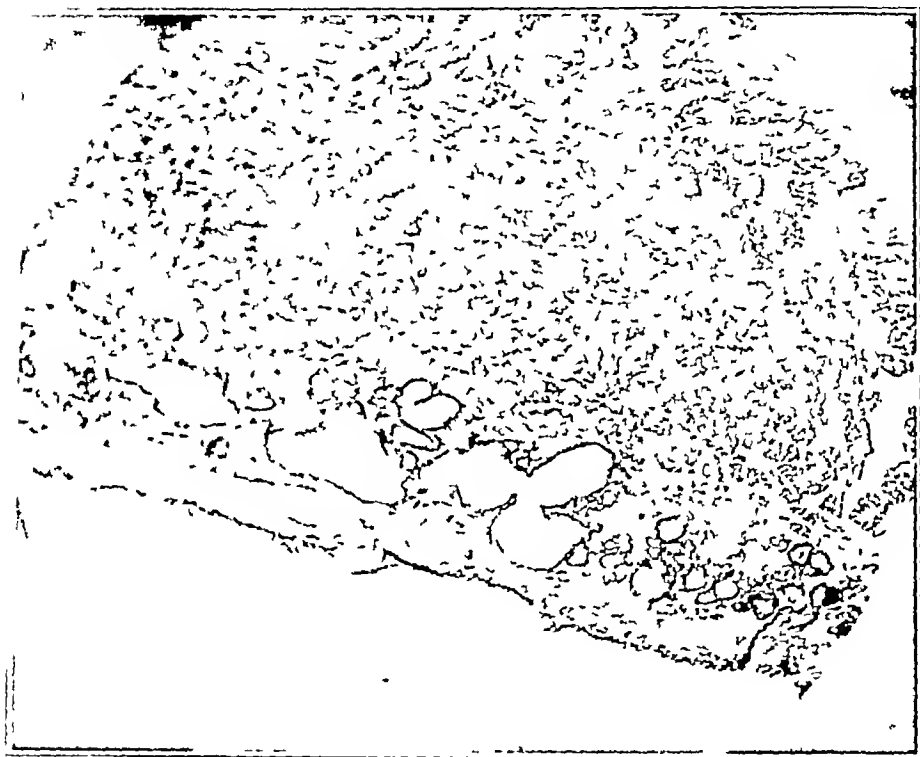


Fig 15—Higher power magnification of figure 14 showing the stroma and absence of microscopic appearance of disintegration (magnification of X 57)

a remission following treatment with iodine demonstrated the range of analyzing all tumors of the thyroid gland in the light of facts in order to interpret properly their pathologic significance. A pathologic study was then made of 1172 cases of nodular goiter which were associated with a variety of symptoms of hyperthyroidism and in which the degree of hyperthyroidism was elevated from 25 to 100 above normal. In 100 cases were of such a degree of severity that the clinical picture was exophthalmic goiter associated with the hyperthyroidism. In the remaining sixty cases the hyperthyroidism was



severity, and a clinical diagnosis of toxic adenoma had been made. The history of these cases was in general that of a nodular goiter associated with hyperthyroidism of long standing.

In nine of the 109 cases (8 per cent), the clinical tumors or nodules resembled true benign parenchymatous neoplasms. These tumors were well defined, not so much by a capsule, but by their microscopic appearance, which was in sharp contrast to the surrounding thyroid parenchyma (fig 14). The great bulk of such a tumor was composed of epithelial tissue supported by a relatively scant stroma. The epithelial

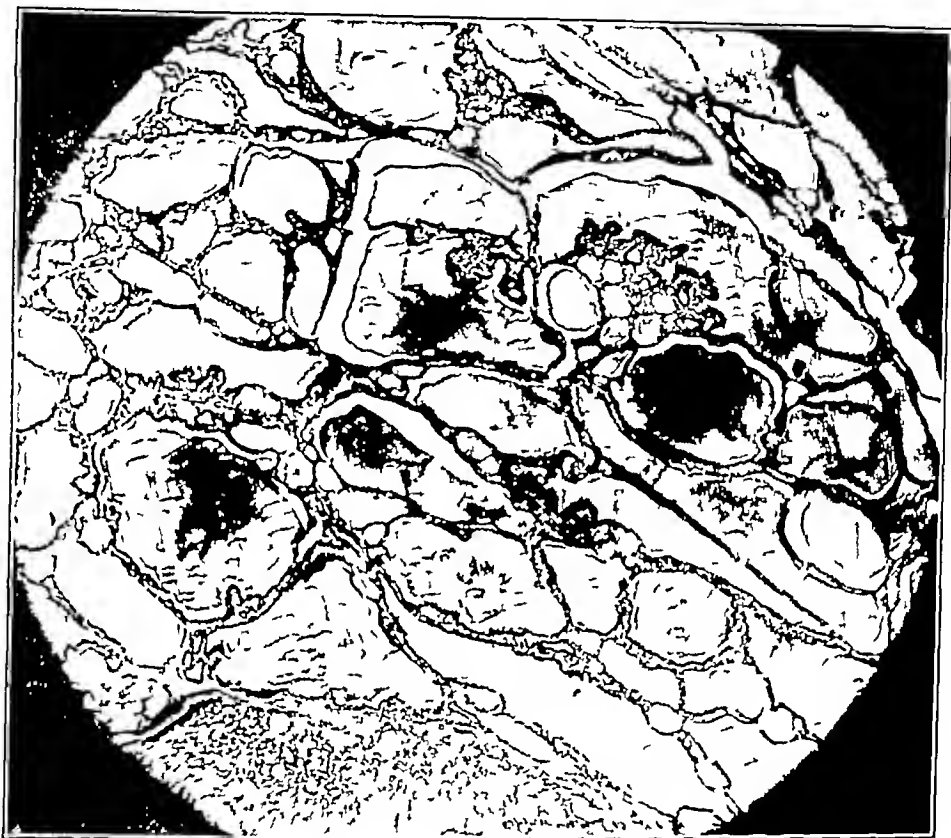


Fig 16—In the lower portion of the photomicrograph a tip of a true benign neoplasm, an adenoma, can be seen. Typical hypertrophy and hyperplasia of thyroid parenchyma surrounding tumor is to be noted. Patient had nodular goiter with exophthalmic syndrome. An artificial iodine remission was established. The thyroid tissue about the neoplasm underwent the average amount of involution, but the histologic appearance of the neoplasm was unaffected. Reduced from a magnification of  $\times 57$ .

cells were, in the main, arranged in narrow anastomosing strands or columns which on examination with the higher power lens proved to be composed of small clusters of epithelium in the form of primitive acini that did not contain a lumen (fig 15). The apexes of the cells abutted on one another, they did not appear to be much increased in size, but were rounder than the cells of the normal adult thyroid parenchyma.

The fourth case observed was that of a child, aged 8, who had extensive pulmonary tuberculosis, operation was not attempted. A fifth case has been seen recently in a thin young woman, aged 18, who was injured in an automobile accident three months prior to examination. A typical deformity was present. There are no symptoms except discomfort on abduction of the arm. She is able to do her work, which is clerical. Her chief complaint is the deformity, and she is still undecided as to whether a scar in this region would be preferable to the present appearance.

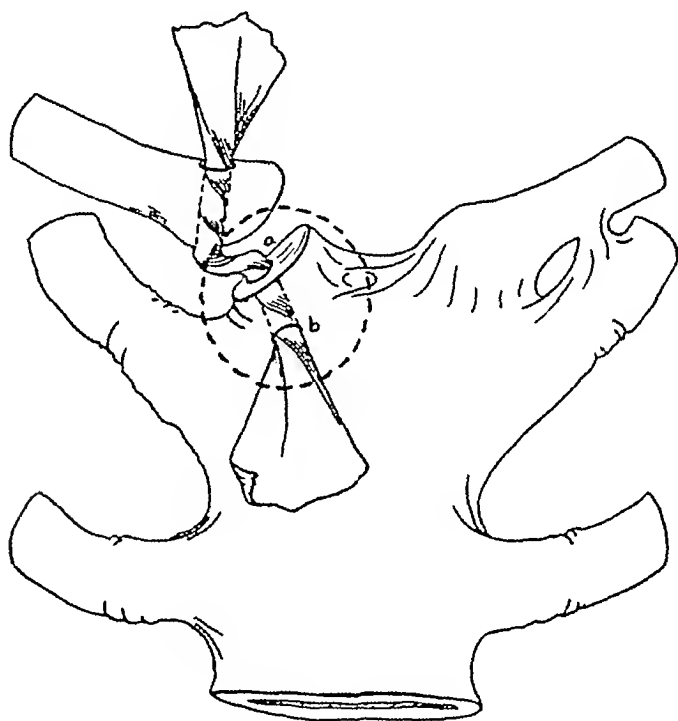


Fig 3—Method of fixing clavicle by drilling the sternal articulation

#### FRACTURE OF THE PATELLA

In this rather common fracture in which operation is the usual procedure, the use of a massive graft of fascia lata seems to be the ideal method of repair. It is desirable to obtain close, accurate and permanent apposition of fragments in such a manner that early motion of the knee joint can be allowed. The end-results by most of the accepted methods of suture are usually good, whether obtained by repair of the capsule and lateral extension tear with chronic catgut or kangaroo tendon or by wiring the fragments together. The capsular suture alone, however, is prone to result in poor approximation of fragments and necessitates several weeks of fixation of the knee joint in extension. refracture or reseparation also has been known to occur.

the joint. The arm was held in extension, and rotation of the forearm was impossible. By gentle traction on the forearm and flexion of the elbow the dislocation was easily reduced.

Operation was advised and accepted. Through a curved incision over the outer aspect of the elbow, the region of the head and neck of the radius and the triangular portion of the upper end of the ulna was exposed. After considerable difficulty, a strip of fascia lata 15 cm wide and 15 cm long was successfully passed around the neck of the radius. This was fenestrated and passed through a 3 mm drill hole in the triangular portion of the ulna, and sutured to itself with several non-absorbable catgut sutures. Gentle motion was started at the end of forty-eight hours. Within four weeks, complete motion had returned, and

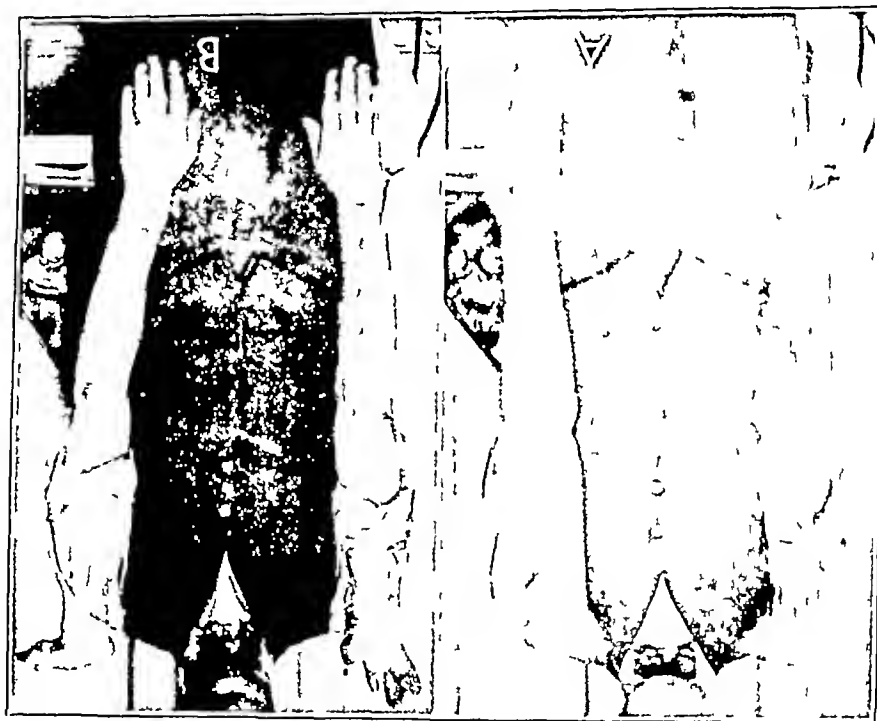


Fig 18—Superimposed exposures of the patient three months after operation for recurrent anterior dislocation of radial head. A complete range of motion is illustrated. *A* indicates the patient in supination, *B*, in pronation.

three months after the operation he was allowed to resume his work. The disability had not recurred a year after the operation.

#### SUMMARY

A method of using massive grafts of fresh, autogenous fascia lata in the repair of certain acute lesions of bones and joints is presented. The technic is simple and does not require any unusual apparatus. Fascia lata in the proposed widths and lengths will withstand as much strain on it as any of the foreign body materials in common use for such procedures. It has the distinct advantage of retaining life and forming a permanent structure.

Prolonged disability is common as a result of the long fixation of the knee joint. For this reason many surgeons have returned to fixation by means of silver or bronze wire. The use of the massive fascial graft gives accurate approximation of fragments and allows immediate active motion of the knee joint. Whether or not real bony union takes place is uncertain but the fragments do not separate with use and owing to the safety of early motion of the joint the disability is reduced to a minimum.

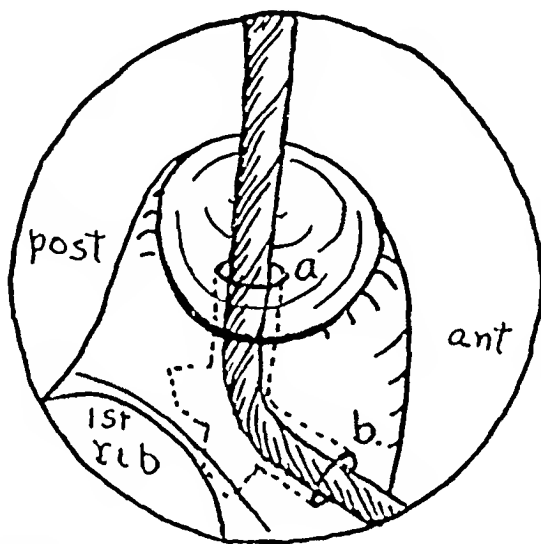
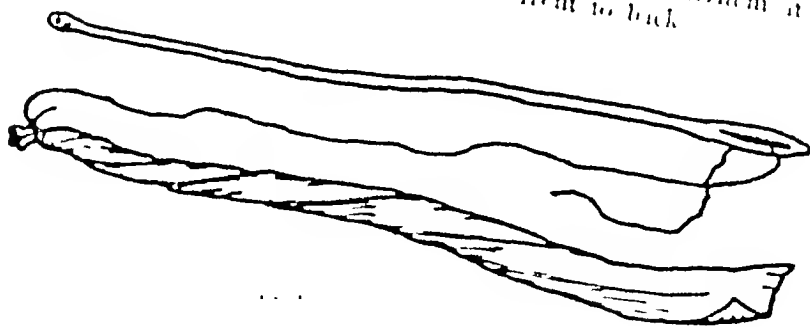


Fig. 4—Lateral view illustrating method of drilling the tibia at a point 'a' to avoid the danger of complete penetration from front to back.



# CONTRACTION OF THE GALLBLADDER IN THE

## COMMON BILIRUBIN (XANTHURUS

### XANTHOSIS) \*

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It is now generally accepted by almost all who study the physiology of the gallbladder that it contracts through the cystic duct. Furthermore, the contraction that it is completed by the contraction of an intrinsic musculature is becoming more and more assured. Recent observations on the gallbladder of man (Levine<sup>1</sup>), as well as the observations of Ivy and (Oldberg<sup>2</sup>) on the effect of secretion on the gallbladder, further substantiate the contractions of many others that the wall of the vesicle does contract and thereby expels bile into the cystic and common duct.

As would be expected, most of the recorded observations on the emptying of the gallbladder have been made on common laboratory mammals, such as the dog, cat, rabbit and guinea-pig, because of their accessibility and because of their higher phylogenetic position with an anatomic organization more closely allied to that of man. Relatively few observations have been made on birds, although I have considerable unpublished data on the contraction of the gallbladder in the hen and on the contraction of the common hepatic duct in the pigeon. The reports of Ivy and Oldberg<sup>2</sup> have observed the gallbladders of a few turtles and frogs. Higgins and Mann (1926<sup>3</sup>), in reporting studies of the gallbladders of dogs and guinea-pigs, recorded a few cursory observations on the biliary vesicle in the garpike (*Lepidosteus*). Generally, however, the lower vertebrates have contributed but few data to the wealth of information hitherto recorded on the functional activity of the extrahepatic biliary tract. Such a dearth of facts is in a measure lamentable, for in these phylogenetically older and less differentiated species fundamental physiologic processes maintain. It is a fact that with increased specialization and subsequent differentiation accompanying the development of higher forms, some modification

\*From the Division of Experimental Medicine and Pathology, The Mayo Foundation  
 1 Levine, Samuel. Contraction of the Gallbladder Seen in Man, Arch Int Med 40 420 (Oct) 1927  
 2 Ivy, A. C., and Oldberg, Eric. Contraction and Evacuation of Gallbladder Caused by Highly Purified "Secretin" Preparation, Proc. Soc. Exper Biol & Med 25 113, 1927  
 3 Higgins, G. M., and Mann, F. C. Observations on the Emptying of the Gallbladder, Am. J. Physiol 78 339 1926

rupted sutures of catgut are inserted. The rent in the lateral extension of the capsule is closed with interrupted no. 2 chromic catgut sutures. It is not necessary to use fascia for these sutures as the tear is through fascial structures which heal readily, once they are approximated, and there can be little, if any, strain on this region, owing to the absolute

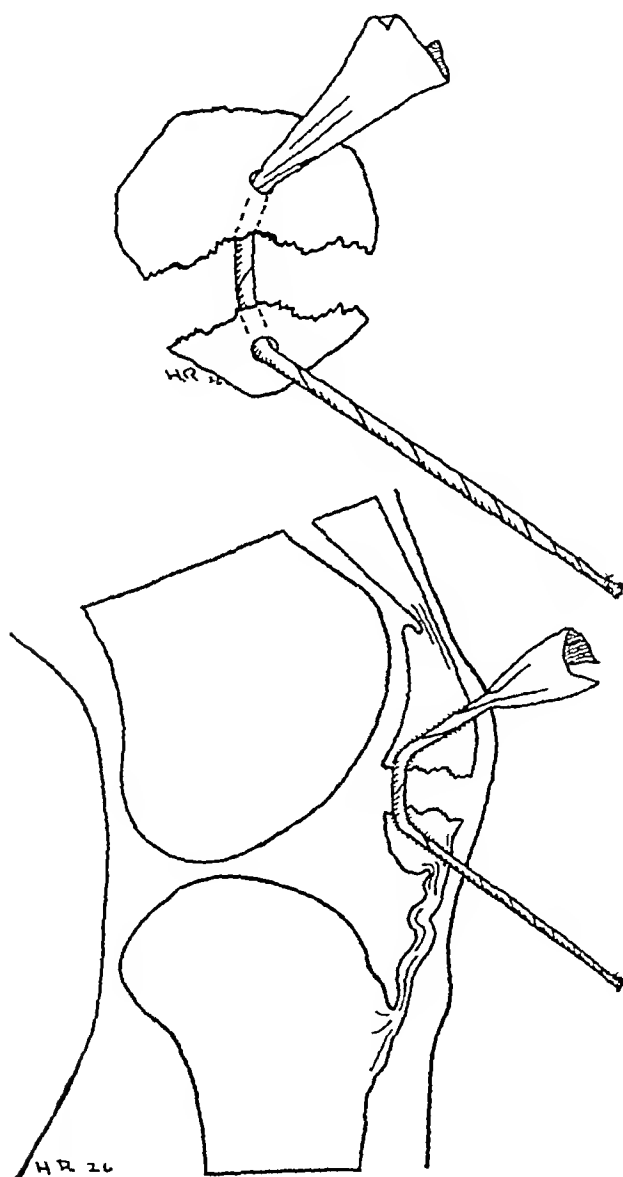


Fig 6—Method used in fracture of the patella. Note the oblique tenestrations in the fragments. The fascia is 3 cm by 24 cm, the drill, 5 mm.

fixation of the fragments of the patella with the fascial graft. Care should be used not to penetrate the joint surface of the patella with the drill. Although in many cases the lower fragment is found badly comminuted, there is usually one principal fragment which can be drilled

of the fundamental body processes may be expected. Nevertheless, a thorough understanding of the fundamental biologic principles that maintain in the lower vertebrates will facilitate the interpretation of the physiologic activities which regularly go on in the mammal.

With the foregoing in mind, a study of the biliary tracts of a large number of fresh-water fishes was undertaken. Through the courtesy of Mr. H. L. Canfield of the United States Bureau of Fisheries at La Crosse, Wis., the entire facilities of the numerous fisheries along the upper Mississippi river were placed at my disposal. With the assistance of the crews employed at the station, a few representative fishes of nearly all the species which inhabit this region were brought to the station laboratory for study. After a preliminary fast the fishes were fed a meal of fat, then, at varying intervals, observations were made on the gallbladder and the extrahepatic biliary tracts. In accordance with existing data on mammalian gallbladders, it was found that in nearly all fishes that were given the meal of fat, the biliary vesicle had emptied within the ensuing two or three hours, and that they were again distended with bile after from four to six hours. In studying as many different species as were available at the station, it appeared that the common bullhead (*Ameiurus nebulosus*), because of the anatomic relations of the gallbladder, liver, common duct and duodenum, would lend itself most suitably to continued observation on the motor activity of the gallbladder and the common bile duct. Again through the courtesy of Mr. Canfield, several cans of these fishes were shipped to Rochester, where they were confined in laboratory tanks equipped with running water, and the following observations were made.

#### ANATOMY OF THE LIVER AND BILIARY TRACT

The liver of the common bullhead is slightly asymmetric and lies in the anterior third of the peritoneal cavity in close contact with the anterior surface to the septum transversum. Although the liver is a single organ, it is composed of two lobes of which the left is somewhat the larger. Each of these two possess smaller anterior, lateral and posterior lobes, thus giving to the margin of the entire organ a somewhat serrate appearance (figs. 1 and 2).

A short esophagus continues posteriorly from the pharynx along the dorsal surface of the liver and between the two main lobes. Slightly posterior to the hilum of the liver, the esophagus continues into a pear-shaped stomach which lies to the left of the median line, posterior and medial to the caudal prolongation of the left lobe of the liver. The stomach continues into the duodenum, which is shaped somewhat like a horseshoe, and makes a wide bend to the right passing through the hilum of the liver, and then posteriorly along the right side of the peritoneum.

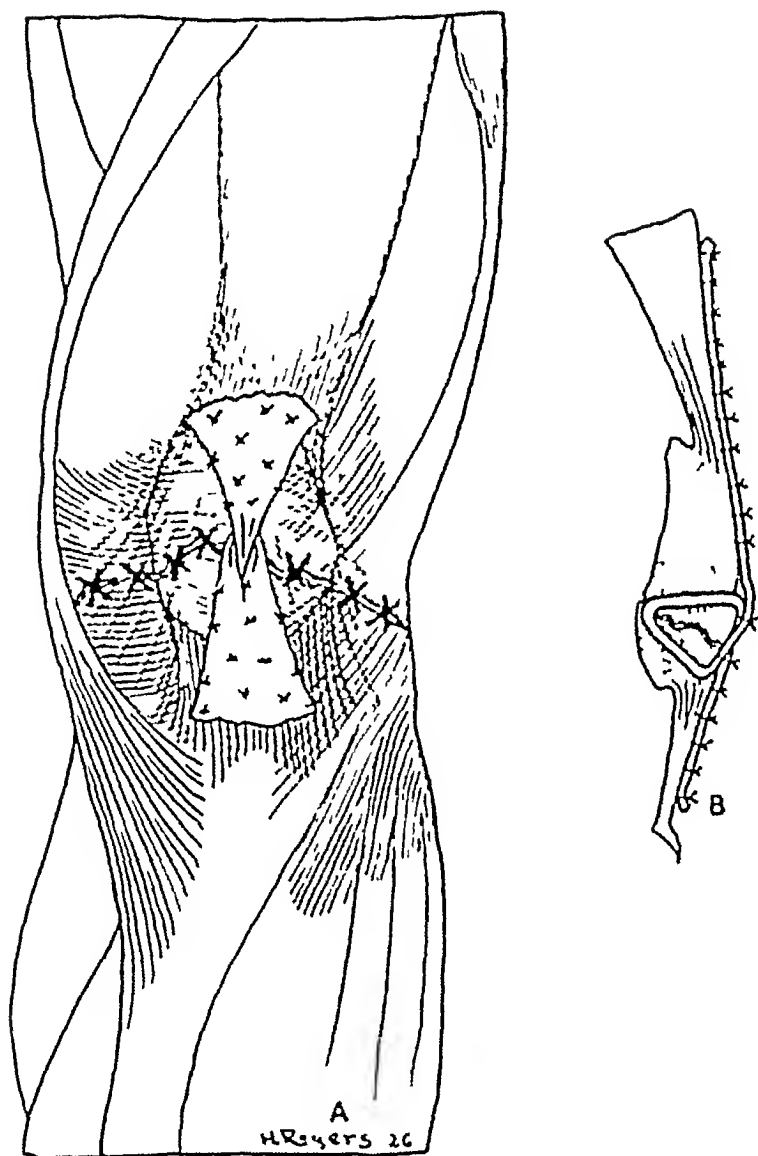


Fig 7—*A* illustrates complete fixation of fracture of the patella. The graft can rarely be too long, as the more of it is sutured to the quadriceps above, and to the prepatellar tendon below, the stronger the fixation. Note the repair of the lateral extension tear with no. 2 chrome cutgut. *B* is a lateral diagram of completed fixation. Note the lack of joint penetration.



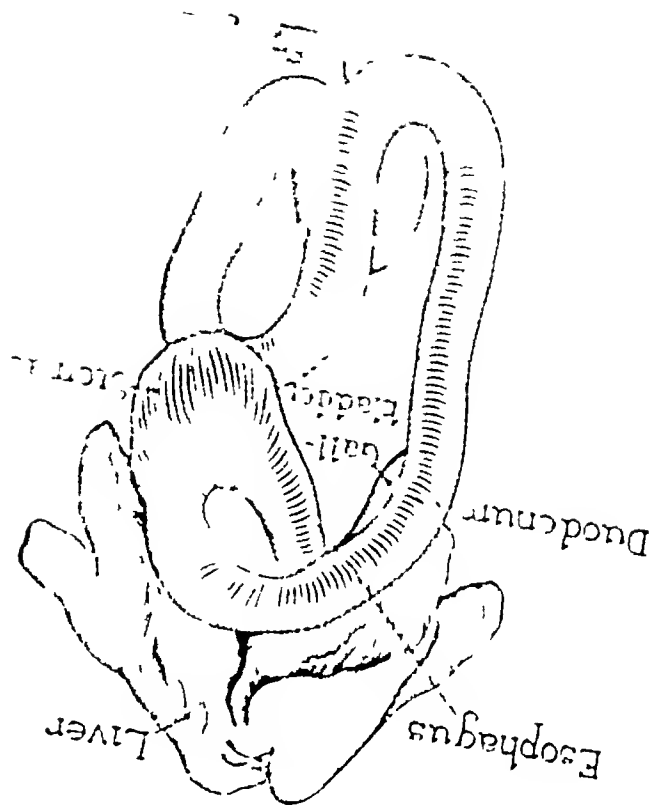


Fig. 1.—The liver, gallbladder and gastro-intestinal tract of the common bill  
bird. The gallbladder is slightly elevated and the bases of the liver reflected



HIGGS—CONTRACTION OF GASTRIC

successfully If such comminution should exist that a fragment of suitable size cannot be found, the graft can be passed beneath the whole of the lower portion and brought out through the patellar tendon immediately below the bone This has not been found necessary in any case as yet The graft is taken from the uninjured thigh for several reasons, principally, because the long wound is prone to interfere with early active motion of the knee joint which is begun the day following operation Also, it is often desirable to have the graft prepared by

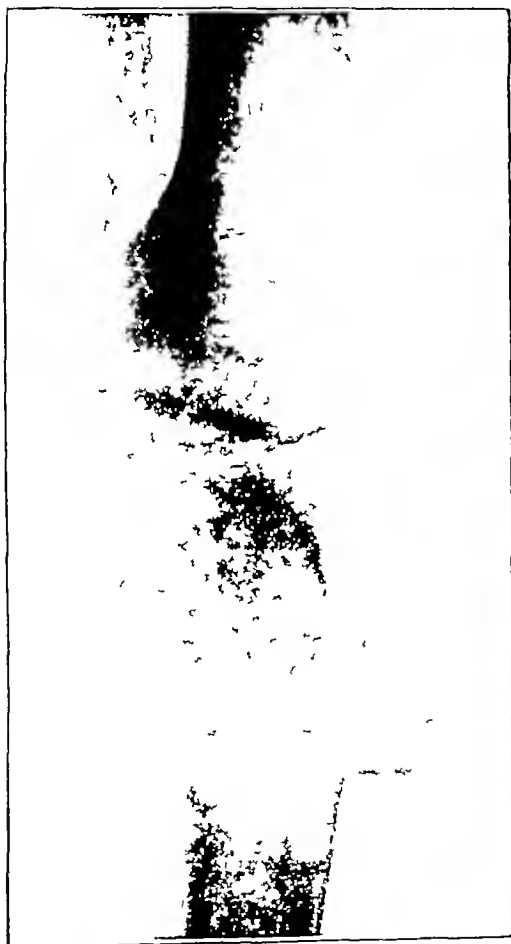


Figure 8



Figure 9

Fig 8—Lateral view of fracture of the patella

Fig 9—Fracture of the patella shown in the preceding figure shortly after fixation by massive fascial graft Note the excellent approximation of fragments

an assistant while the patellar fragments are being exposed and drilled Flexion of the knee beyond 90 degrees should be obtained in less than twelve weeks Walking should be allowed at the end of four weeks, at first with crutches, weight bearing being gradually allowed to the point of discomfort After ten weeks, aid should not be needed in walking

The gallbladder and the extrahepatic biliary tract lie within the portal area, between the liver and the duodenum. The gallbladder lies on the right side of the peritoneal cavity, just dorsal to the descending limb of the duodenum and posterior to the right lobe of the liver, but relatively free from it. It is supported in position by the hepatoduodenal omentum through which several venous channels pass from the intestine by way of the gallbladder to the liver. From six to eight hepatic ducts of varying size empty into an elongated common duct which pursues an arcuate course along the inferior surface of the liver from the neck of the gallbladder to the dorsal surface of the duodenum, 12 mm from the pylorus. A large hepatic duct, occasionally double, which drains the main portion of the right lobe of the liver,

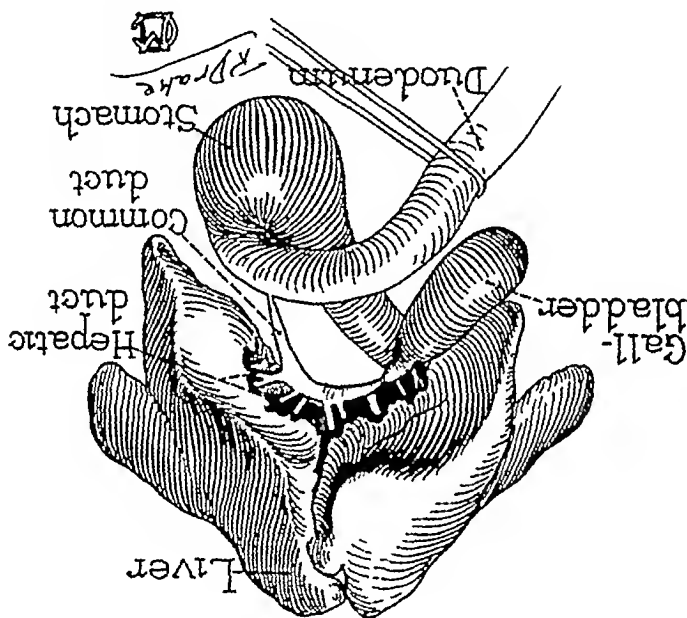


Fig 3—Partial dissection of the extrahepatic biliary tract in the common bullhead

The remnant appears to empty directly into the neck of the gallbladder. In the upper portion of the common duct, from about 3 to 5 mm distal from the gallbladder, there is a restricted region which usually appears to be in a state of greater tonus than any other portion of the hepatic tract. From this point the dimensions of the common bile duct increase in both directions, and this portion of the hepatic system seems to bear some significant relationship to the physiologic responses that ensue on a fat meal. The common duct from the neck of the gallbladder to the duodenum, when in a state of rest, varies from 18 to 25 mm in length among the different fishes examined. Its greatest diameter, about 2.5 mm, is near the

## FRACTURE OF THE OCCIPITAL

Open reduction of this fracture is becoming more popular following comparative studies of end-results. In cases in which gross separation of fragments has occurred inability to obtain a satisfactory reduction and the long period of fixation in extension necessary to obtain union have brought about more radical measures. The time element of dysfunction has been longer than it should be in many of these cases, and some type of fixation should be used that allows early active



Fig. 10—Since in figures 8 and 9 three months after fixation, the patient is now walking. There has not been any tendency for fragments to separate.

motion of the joint. Suture of the torn capsule with ordinary suture material gives good approximation of fragments, but motion must be delayed and reseparation of fragments may occur. Fixation with wire or pegs may allow early motion, but frequently necessitates a second operation for removal of the foreign body. Fixation by means of fascia lata is more nearly ideal than by these other methods. Three patients have been treated in this way so far. Wire had been used previously in the first case, the wire breaking, allowing reseparation at the end of

junction of the left hepatic duct from which point in growth the cords extend until at the duodenum the duct is approximately 0.5 mm in diameter.

The venous drainage of the gastro-intestinal tract is usually large for so small an animal (fig. 4). The hepatic portal vein carries most of the venous blood from the intestine to the liver but in addition numerous smaller venous channels continue unimpeded into the horizontal and the descending portions of the duodenum to the liver.

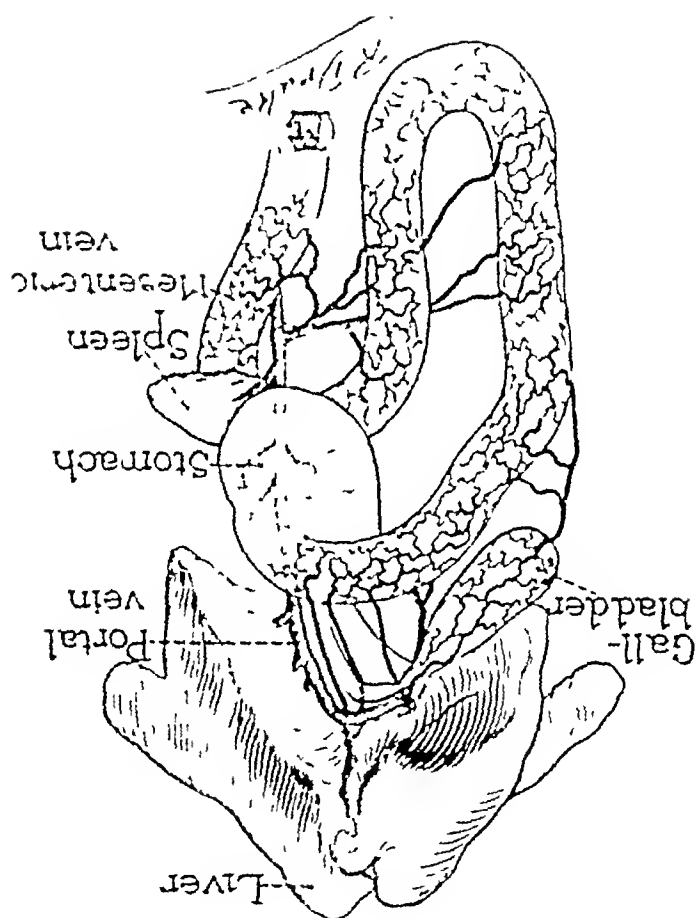




Fig 11—Patient whose roentgenograms are shown in figures 8, 9 and 10, showing amount of active flexion at the end of three months. Note the absence of scar from the thigh on this side. The fascia is taken from the opposite thigh.

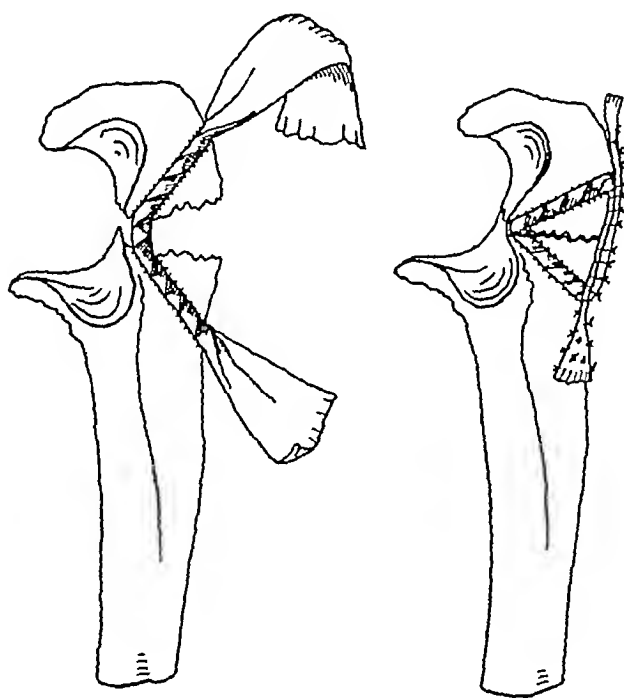


Fig 12—Method of fixation of fracture of the olecranon. Care is taken not to penetrate the joint with the drill. The graft is 2 cm by 20 cm, the drill, 3 mm in diameter. The operation is completed as in figure 7 1 of the patella.

and the dorsal surface of the pylorus. The main channel then continues medially along the inferior surface of the left lobe of the liver and in its course gives off four main veins which enter the substance of the liver while its ultimate distribution is to the inferior surface of the right lobe of the liver where it bifurcates into two main channels which enter the right lobe near the neck of the gallbladder. The veins which drain the ventral wall of the stomach, the duodenum near the pylorus, and the common bile duct, all course independently forward to empty into the portal vein on the inferior surface of the left lobe of the liver. The remaining portion of the duodenum, however, down to within 50 mm of the pylorus, is drained by from three to five independent veins which course obliquely forward into the region of the junction of the gallbladder with the common bile duct and then empty into the portal circulation of this side. The venous distribution is unique in the sense that the radicles carrying the blood from the anterior 50 mm of the duodenum do not have any relation with the hepatic portal system as such, but course independently forward and appear to be definitely associated with the venous drainage of the gallbladder.

With few exceptions, the foregoing description of the anatomic relations of the liver, the gastro-intestinal tract and the related blood supply is most commonly encountered. In this study of seventy-five fishes, however, one fish was opened in which there was complete reversal of the organs of the peritoneal cavity. The lobes of the liver were of the usual proportions, but the larger one was on the right side. Likewise, the pear-shaped stomach was on the right side and the duodenum made the usual broad curve from the pylorus on the right up through the hilum of the liver around to the left side of the peritoneum. The gallbladder was directly below this descending limb of the duodenum, it was slightly larger than the normal vesicle, but was joined to the usual extrahepatic biliary system, all of which was reversed.

#### THE EMPTYING OF THE GALLBLADDER

A phase of this study which is strikingly significant in the light of the present controversy on the emptying of the gallbladder is the contraction activity of the organ in response to a meal of fat. Since the gallbladder is free from the liver and may readily be exposed by simple traction on the duodenum, it is a simple procedure to open the fish, expose the vesicle and observe it for prolonged periods (fig. 5). Early in this study it became evident that the usual physiologic processes would go on only when the viscera so exposed were bathed in a physiologic solution of sodium chloride. Various solutions were tried including Ringer's and Tyndes, but perhaps the more satisfactory results were attained by 0.6 per cent solution of sodium chloride in tap

ten weeks. The massive graft of fascia lata is used as in the patella. Here again care is taken to pass the drill obliquely so as to prevent penetration of the articular surface (fig. 12). A slightly curved incision is used through the soft parts in order to protect most of the graft from the superficial suture line. Motion is started almost immediately, with gratifying results as regards length of disability and complete restoration of function. A 3 mm. drill is used and a strip of fascia 2 cm. in width and 20 cm. in length is sutured to the triceps tendon and fascia above, and to the tarsi of the forearm below with chrome catgut (O) sutures. The torn capsule is sutured with interrupted no. 1 chrome catgut.



Fig. 13—Fracture of the olecranon. The tremendous swelling is due to primary treatment with straight splint applied with adhesive tape. The arm was suspended until the swelling subsided. Fascia lata fixation was performed two weeks after injury.

#### RECURRENT ANTERIOR SUBLUXATION OF THE RADIAL HEAD

A relaxation or a rupture of the orbicular ligament, sufficient to allow the radial head to luxate repeatedly, is an uncommon occurrence in our experience. The one case observed follows.

A thin, healthy, muscular American man, aged 21, while lifting the end of a heavy packing case felt a sudden snapping in his elbow. He was immediately disabled and in great pain with his arm extended, flexion at the elbow and rotation of the forearm being impossible. A physician was called who manipulated the arm without an anesthetic, during which a click was heard followed by



water to still content of the latter being usually high. I was forced to stop during these observations to relieve pains of vertigo, and although the bubble is unusually hard it is less sensitive to the loss of aeration and consequently many insects were killed by the carbonic acid. Numerous methods were tried but the one which was finally resorted to and which has proved satisfactory was the use of 60 per cent sodium chloride in tap water. This solution is oxygenated, passes by gravity through a two-way cock into a capillary and into the mouth of the animal. The fluid bubbles the gills and passes back over the viscera and then out of the tube through the second aperture. A constant stream of oxygenated solution passes over



immediate comfort and restoration of motion. A sling was applied and within a few days the man returned to his work. A short time afterward, while producing the same strain, a recurrence of his disability took place. This time the patient and his fellow workmen managed the manipulation successfully, and the man kept at work, favoring his arm as much as possible. After a third recurrence, he applied for treatment.

On examination, the arms were identical in appearance. There was no swelling or discoloration. There was complete motion in all directions and he seemed to be able to hyperextend all his joints. There was no demonstrable tenderness. A roentgenogram failed to show any abnormality. As his disability had always resulted from lifting while his arm was extended, a plaster of paris cast was applied from the wrist to the axilla with elbow held at right angles. With this



Figure 14



Figure 15

Fig 14—Fracture of the olecranon shown in preceding figure, after fascial fixation

Fig 15—Fracture of the olecranon, shown in two preceding figures, four weeks after fascial fixation, six weeks after injury

the man continued at his work as best he could. The shell was removed at the end of six weeks, and aside from some muscular atrophy, the arm seemed to be normal. In a few days, however, he returned with the story that the condition had recurred during the night, awakening him from sleep. After considerable difficulty, he was able to restore the motion and regain comfort. At this time, ecchymosis or swelling about the elbow was not evident. There was normal motion in all directions. By reproducing the lifting strain, the man was able to demonstrate his lesion. There was a sudden fulness in the anterior cubital space, associated with a depression over the head of the radius on the lateral aspect of

is well distended and the extrahepatic biliary tract is easily recognized into the duodenum, about 1 cm from the pylorus. Immediately, peristalsis of the duodenum is set up. This may have its inception at the point of puncture, or, as often happens, complete contraction of the duodenum occurs at a level 40 mm below the pylorus. From this point a wave continues posteriorly along the intestine, an antiperistaltic wave also usually passes backward to the pylorus. Active peristalsis and antiperistalsis then ensue. Many waves may arise at the pylorus, while others may arise at various distal points and travel in both directions for varying distances. Frequently, too, peristaltic waves are set up in the stomach. These arise in the region of the posterior fundus and the entire stomach is laterally crowded up against the pylorus. This is a reflex response on the part of the stomach, for during the peristaltic activity of the duodenum the pyloric sphincter has remained intact, and regurgitation into the stomach has not occurred, for the latter remains pale and flaccid while the duodenum is markedly colored by the injected fat.

During the rather extensive duodenal activity in which peristaltic waves have passed repeatedly over the orifice of the common bile duct, there has been no effect on the gallbladder. The entire extrahepatic biliary tract has remained inactive so far as any muscular movement is concerned, and it may be positively concluded that peristalsis does not have any inciting influence on the discharge of bile from the gallbladder. As the injected fat is gradually forced posteriorly, peristalsis of the duodenum becomes less frequent. After thirty minutes an additional 2 cc of egg-yolk and cream is given in the same way, and again the duodenum becomes active with waves of varying strength and duration. At the end of an hour 2 cc more is given, so that 6 cc of fat constitutes the test meal. As yet there is no indication that the gallbladder will become active, for it hangs just dorsal to the duodenum well distended with bile, its walls somewhat flaccid and without tone. The more or less forceful movements of the duodenum which is in contact with the ventral wall of the vesicle fail to induce movement within the gallbladder. Gradually, however, at intervals after giving the first 2 cc of fat, ranging from an hour and fifteen minutes to an hour and forty-five minutes, an initial tonus is discernible over the entire surface of the gallbladder. There is no movement as yet, but the flaccidity is lost and the wall becomes tense and frequently somewhat lighter. At this time, too, there is slight evidence of contraction in the upper part of the common duct. If the overhanging lobes of the liver are now gently retracted so as to avoid mechanical irritation, marked constriction of the upper common bile duct, about 3 mm



Fig 16—Photograph of patient whose roentgenograms are shown in figures 13, 14 and 15, taken four weeks after fascial suture of the olecranon. The superimposed exposures show the amount of flexion and extension of elbow. The patient was allowed to return to moderately heavy work six weeks after operation.

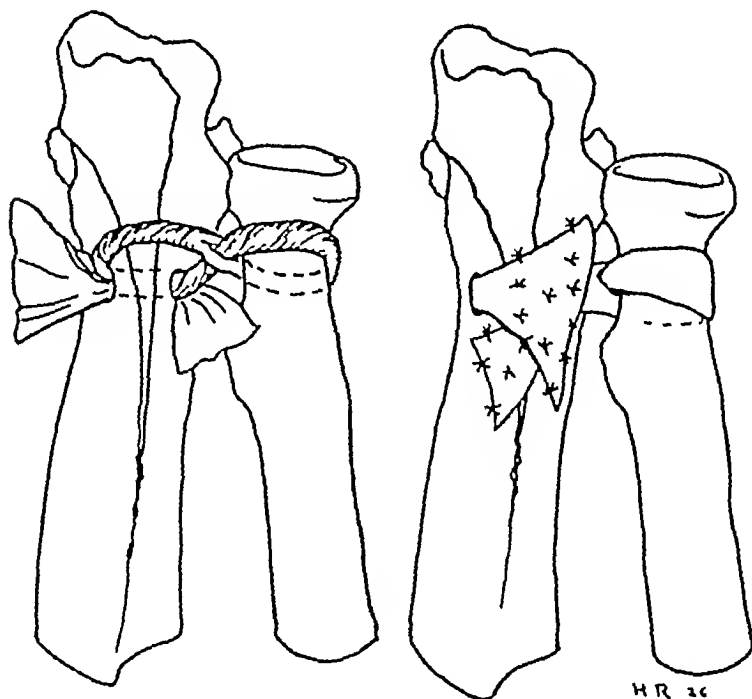


Fig 17—Schematic representation of method used in substituting a fascial graft for the orbicular ligament in the case of recurrent anterior dislocation of the radial head.

from the gallbladder may be recognized. The constriction of this region of the duct together with the onset of tonus over the wall of the gallbladder are the first indications that muscular activity of the biliary tract is likely to follow soon.

Generally within fifteen minutes after the onset of tonus in the gallbladder, contraction waves are visible over the entire vesicle and the common bile duct as well. These waves appear to have their origin at the restricted region of the common bile duct about 3 mm from the neck of the gallbladder. From this point of departure these waves pass over the common duct completely forcing out the bile within the duct into the duodenum. Further coincidence with this duct wave, or frequently just after it a wave arising from the same region passes in the reverse direction over the gallbladder, forcing out a quantity of bile into the common bile duct. These waves, then, originate in the common duct and pass over the neck of the gallbladder to involve the fundus as well. Each wave need not be complete in the sense that it involves the entire vesicle, frequently it may fade out after traversing

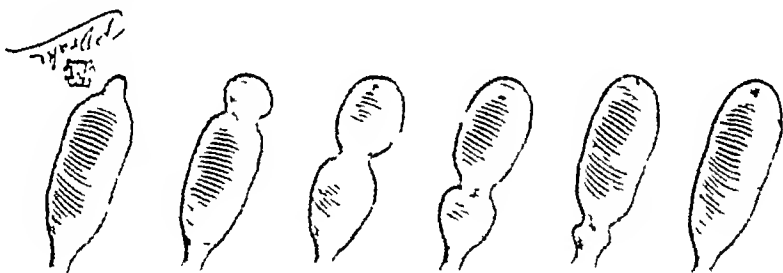


Fig. 6.—A single contraction wave passing over the gallbladder following onset of tonus.

over a half or third of the gallbladder. The picture that now presents itself is perhaps more aptly illustrated by that of a toy balloon. If one were to draw this balloon through a small loop which represents the contraction wave, the appearance would be much like that in the gallbladder of the fish during motor activity (fig. 6). All the contraction waves, however, do not travel in the reverse direction. Frequently after the contractile mechanism has been set in motion, by factors as yet undetermined, independent waves of contraction may arise at almost any level on the gallbladder and travel in both directions. They frequently begin at the fundus and travel part way or entirely over the gallbladder, expelling more bile into the common duct. Furthermore these contractions need not always involve the entire diameter of the vesicle at any one level, for occasionally the contractile area may be restricted to only a small portion of the wall, so that peculiar and much distorted figures of an otherwise oval gallbladder are occasionally seen during the motor activity. There does not appear



benign neoplasm. The microscopic structure suggested an extreme degree of cellular proliferation and regeneration with the actual formation of new tissue. In these tumors, there was not the slightest suggestion of degeneration or histologic regression indicating involution. The typical histologic changes denoting hypertrophy and hyperplasia, however, were found in the parenchyma of the thyroid surrounding these tumors and throughout the remainder of the gland (fig 16). In



Fig 18—Another section from same case as in figure 17. Papillomatous infolding of epithelium is more pronounced. Typical involutional tumor which has again assumed the appearance of exophthalmic goiter. Reduced from a magnification of  $\times 57$ .

these cases, therefore, it would seem far-fetched, to regard the benign neoplasms as the cause of the hyperthyroidism rather than as coincidental pathologic lesions.

In thirty-seven cases (34 per cent), the nodular element was composed of colloid cysts (figs 11, 12 and 13), encapsulated areas of dilated

to be any definite synchronous activity between the motor mechanism of the common duct and that of the gallbladder. Successive contraction waves have been observed to pass over the common duct, unaccompanied by any visible contraction of the gallbladder. Then, too, contraction waves of variable extent may involve all or a part of the gallbladder without any visible motor activity of the common duct. However, in what have been thought to be thoroughly healthy and vigorous animals, both common duct and gallbladder become contractile at about the same time following the ingestion of fats and remain so for a considerable period.

The waves of contraction in both the gallbladder and the common duct do not follow each other in rapid succession. I have often tried to determine the time interval between these successive contractions, but the frequency varies in the same animal and in different animals, dependent no doubt on certain undetermined physiologic factors. Usually such contractions follow each other at from two-minute to four-minute intervals. Although the waves are not frequent, when they once appear they traverse either the common duct or the gallbladder at a rate as rapid as the normal peristalsis of the duodenum. Throughout this period of motor activity of the common bile duct and the gallbladder, the duodenum, except for occasional peristaltic movements, has been inactive. Thus the movement of the biliary tract is independent of the activity of the duodenum, and the gallbladder empties without the so-called sucking of the contracting duodenum.

The gallbladder may empty itself completely, it has often been noted on opening an animal that it was entirely void of bile appearing contracted to not more than 2 or 3 mm in diameter and to 8 or 10 mm in length. This degree of emptying was never experienced in animals under observation. Although small amounts of bile were ejected with each contraction wave, the gallbladder usually failed to contract to less than one third of its original size. Gradually the waves become more infrequent and finally cease entirely, although considerable bile may still remain within the gallbladder. The accountable factors in the cessation of the flow of bile are unknown. Fatigue or confinement may be a factor, and yet when the fish is taken from the tank it is still vigorous and given to the usual habits of jumping and splashing. These fishes do not withstand laboratory confinement in the same way or so satisfactorily as do those of the ganoid group. I have retained garpike in laboratory tanks for long periods, but the bullhead gradually loses vigor and becomes inactive even though aerated water and food are provided. This marked lassitude is reflected in the physiologic response of the biliary mechanism to the usual meal of fat. Fishes that have been retained in laboratory tanks for two weeks are less likely to show marked motor activity of the biliary tract following



Cotton<sup>5</sup> recently reported five cases of pyogenic joints, in three of which there were infections with *Staphylococcus aureus*. He irrigated these with 1 to 15,000 mercuric chloride in salt solution, and the joints became normal. He said that so long as infection was confined to the synovial cavity, the joint was sterilizable. The question arises as to whether the mechanical cleansing is not the main factor in this treatment. In 1925, Gatch, Trusler and Owen,<sup>6</sup> experimenting with intravenous injections into rabbits, showed that of a number of preparations of gentian violet the least toxic was physiologic sodium chloride solution. It was also shown that gentian violet in isotonic 4 per cent dextrose possessed less toxicity than gentian violet in distilled water. Gentian violet had a solubility of 39 per cent in physiologic sodium chloride solution compared to 94 per cent in distilled water. They concluded that gentian violet would exert a temporary bacteriostatic action in septicemia, but that the ultimate benefits depended on the resistive powers of the patient.

In 1925, Brill and Myers<sup>7</sup> showed that a blood medium made up with gentian violet to a dilution of 1 to 10,000 would kill the growth of a *Staphylococcus albus* organism only after twenty-four hours' contact. In reviewing the literature on experimental arthritis, no reference can be found to joints infected with staphylococcus. All the experimentation has been with strains of streptococcus, mostly of the viridans type. A most interesting and instructive piece of work was done by Jackson<sup>8</sup> in 1913. Rabbits were given intravenous injections of a culture of streptococcus, and studies were made of the joints in from two hours to four months after infection. It was shown that after two hours the streptococcus could be demonstrated in the vessels of the perarticular tissues. In ten hours intravascular collections of leukocytes were present. In twenty-four hours there was an exudation and migration of the leukocytes into the joint cavity. Thus, there was an incubation period of twenty-four hours between the time of the intravenous injection of the streptococcus and the time the joint becomes infected. The changes were only those consistent with the varying phases of a single inflammatory process. The changes depended on the independent localization of the bacteria in the joint cavity, in the tissues

5 Cotton, F. J. Bone & Joint Surg. 8:395, 1926.

6 Gatch, W. D., Trusler, H. M., and Owen, J. E. Treatment of General

Septicemia by Gentian Violet and Mercurochrome-220 Soluble, J. A. M. A. 85

894 (Sept. 19) 1925.

7 Brill, I. C., and Myers, H. B. Mercurochrome-220 Soluble and Gentian

Violet, Bactericidal Efficiency by Intravenous Route. J. A. M. A. 84:879

(March 21) 1925.

8 Jackson, Leila. J. Infect. Dis. 12:364, 1913.

a meal of fat than those observed immediately on their arrival at the laboratory. In certain fishes this confined, I have failed to observe any response to the fat, while in others, contraction waves of the common duct were faintly visible, but only after a prolonged interval following the administration of the meal. Obviously, then, to secure the best results, only healthy, vigorous fishes should be used, and these soon after they reach the laboratory.

#### HISTOLOGY OF THE INTRAHEPATIC BILIARY TRACT

The gallbladder is an extremely delicate organ, but, nevertheless, following proper stimulation, it possesses sufficient contractile tissue to eject bile. In the extended condition, the wall in the region of the fundus is slightly more than one fiftieth of a millimeter thick. The mucosa, which comprises a little less than one half of the entire thickness of the wall, is composed of characteristic columnar epithelium of tall narrow cells with nuclei in the base. Differential staining shows that the remainder of the wall is a composite structure of connective tissue and muscle fibers interspersed with abundant vascular channels. There appears to be considerable interlacing of the two tissues, but most of the muscle fibers are grouped into a compact layer coursing in the circular direction and supported on the sides by connective tissue fibrils. In the neck of the gallbladder, the muscle fibers are more loosely arranged, and here it is easy to identify a narrow band of longitudinal muscle fibers and diagonal fibers, as well as those running around the vesicle. The longitudinal fibers are interspersed with connective tissue fibers.

There is gradual reduction in the proportions of the tract passing from the gallbladder to the common bile duct, but the tissues of one continue imperceptibly into those of the other. Within the upper portion of the duct a conspicuous band of muscle fibers, both circular and longitudinal, lies just external to an equally prominent layer of connective tissue, which is separated from high columnar epithelium by a thin basement membrane.

Grossly, the hepatic ducts which drain the right lobe of the liver appear to empty into the neck of the gallbladder. This is not actually true, for they penetrate only the serosal and muscular tunics of the vesicle and then continue posteriorly within the connective tissue of the duct just external to the mucosa (fig. 7). In some cases these hepatic ducts extend for 2 mm. or more within the intramural portion of the cystic duct before emptying into its lumen. In this connection, it may be noted that the tissue of the hepatic ducts resembles the rest of the biliary tract, with especially prominent circular and longitudinal bands of muscle. When the wall of the cystic duct is penetrated, however, it is found that all muscle tissue of the hepatic duct discon-

surrounding the blood vessels of the synovial membrane, in the plicae synovialis, in the tendon sheaths and in the blood vessels of the periosteum and bone marrow near the epiphyseal cartilage. The involvement of the perisynovial and parasyovial structures was marked, and some nodular formation was found in the tissues about the joint. In 1915, Faber<sup>9</sup> showed that by a process of first injecting small quantities of a culture of *Staphylococcus aureus* into the joint, and of following this with one intravenous injection, arthritis could be caused constantly. Without previous sensitization of the joint, two or three intravenous injections were required to cause the arthritis. In 1914, Rothschild and Thalheimer<sup>10</sup> showed that after intravenous injections of a *Streptococcus mitis*, arthritis was caused in 50 per cent of the rabbits experimentally with and that the organism could be recovered from one third of the affected joints.

ORIGIN OF INFECTIONS

First, the knee joint of the rabbit was directly infected by an instillation of 0.1 cc of a twenty-four hour broth culture of a pure strain of *Staphylococcus aureus*. Second, when a definite local reaction was present in the knee, manifested by increase in local heat, swelling and limitation of motion, the joint was aspirated for culture and gentian violet was injected. The clinical manifestations in the joint were followed until the active process had subsided. During this period roentgenograms were taken. Frequent aspirations of the joint for culture were made. The animal was then killed, and the joint studied grossly and microscopically. From one to three injections of gentian violet of 1 cc each were made following the infection. The gentian violet was used in strengths of 1 to 400 (0.25 per cent) and 1 to 200 (0.5 per cent). It was prepared in three different mediums, namely, distilled water, 4 per cent dextrose and olive oil. Thirty rabbits were used in the problem. Attempts were made to sterilize the infected knee joints of 20 of these. This was successful in seventeen, or 85 per cent of the cases. Four rabbits were used as *Staphylococcus aureus* controls, and three as gentian violet controls. Three rabbits died of intercurrent causes soon after the onset of the infection, one from an infection of the blood stream one from a severe diarrhoea following the instillation of the gentian and one from an unknown cause.

The report of the experimental work is divided into four parts, namely bacteriologic, clinical, roentgenologic and pathologic.

9 Faber, H. K. J. Exper. Med. 22: 615, 1915.

10 Rothschild and Thalheimer. J. Exper. Med. 19: 444, 1914.

tinues, so that within the intramural portion of the upper part of the common bile duct, the hepatic ducts consist of columnar epithelium only, supported by a wide band of connective tissue. There are numerous small hepatic ducts, and as many as four of these have been observed to enter the wall of the major duct and course independently into its lumen (fig 7)



Fig 7—Partial cross-section of the neck of the gallbladder shows four hepatic ducts coursing within the connective tissue, between the mucosa and muscular tunics,  $\times 220$

The anterior group of hepatic ducts which drain the right lobe of the liver empty into the lumen of the common duct within the region which is essentially active after the meal of fat. A constricted region of the upper part of the hepatic tract has been described from which as a center, contraction waves pass over the common duct and distally over the gallbladder. Sections of the tract at this point do not reveal

## BACTERIOLOGIC STUDY

A study was made of twenty-four infected joints. Seventeen were successfully sterilized, three were unsuccessfully sterilized and four were controls.

1 *Successfully Sterilized*—These joints required from one to fifty-three days for the sterilization. The time depended on the frequency of administration, the strength and the medium of the gentian violet. They are divided into four groups, according to the gentian violet preparation used.

(a) 0.25 Per Cent Aqueous Gentian. Four rabbits were given from two to three injections in from one to twenty-one days after infection. The joints were sterile in from nineteen to fifty-three days, the average being twenty-one days. Two rabbits which did not show bacteriologic evidence of infection, but did show clinical evidence, were given one injection each. These showed a complete subsidence of the acute condition of the joints in a few days' time.

(b) 0.25 Per Cent Dextrose Gentian. Three rabbits were given from one to two injections in from one to three days after infection. The joints were sterile in from four to twenty-eight days, the average being thirteen days.

(c) 0.5 Per Cent Dextrose Gentian. Four rabbits were given from two to three injections in from one to three days after infection. The joints were sterile in from two to four days, the average being three days.

(d) 0.5 Per Cent Olive Oil Gentian. Four rabbits were given three injections in from one to four days after infection. The joints were sterile in from fifteen to twenty-nine days, the average being twenty-two days.

2 *Unsuccessfully Sterilized*—One animal received two injections of 0.25 per cent aqueous gentian in two and four days after infection. Two received two injections each of 0.25 per cent dextrose gentian in from one to five days after infection. One of the latter two showed a negative culture at the end of ten days, but later on the twenty-eighth and thirty-second day positive cultures were obtained.

3 *Control Staphylococcus aureus*—The four rabbits in this group showed positive cultures. One of these, however, had a negative culture on the twenty-eighth day, but later on the forty-second day at autopsy the culture was positive.

## CLINICAL STUDY

The most important clinical evidence of infection noted were the limitation of motion, the swelling and the increase in local heat. The first two signs were the most exact and had the most relative value in the making of a comparison of the amount of clinical activity in the joints. The limitation of motion is reported in degrees of limitation of extension, for instance, a joint capable of extension only to a right angle is reported as 90 degree limitation of extension. The limitation of motion is placed in the following four groups: (1) between 0 and 10 degrees, (2) between 10 and 60 degrees, (3) between 60 and 90 degrees, and (4) between 90 and 135 degrees. The amount of swelling is reported as slight, fair, moderate or large. The last examination of the knee in the living animal is used in the analysis, as shown

essential differences from the region immediately above or below, but a study of the distribution of nerves to this area, now in progress, may be instructive. The layer of muscle is more compact, however, and circular and longitudinal fibrils intermingle freely with a preponderance of the circular external to the longitudinal, but the layer of connective tissue immediately beneath the muscle is more loosely bound and more

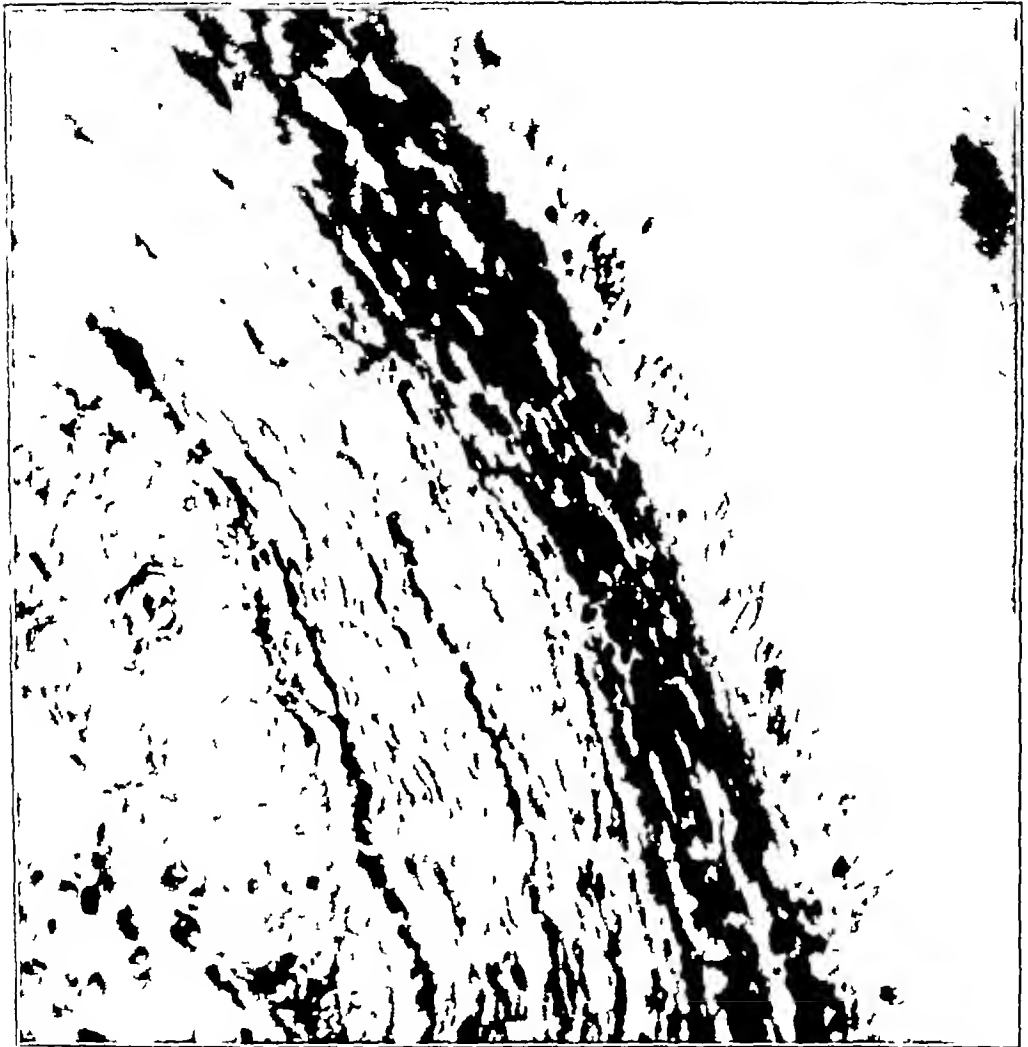


Fig 8—Partial cross-section of the wall of the common bile duct shows the wide band of muscle fibers external to the connective tissue layer,  $\times 570$

hyperemic than elsewhere. The cells of the mucosa are more compressed than in other parts, a condition probably induced by the tonus of the muscle tunic at the time of fixation.

From this constricted portion of the hepatic tract, which perhaps could well be said to be the site of confluence of the neck of the gallbladder with the common duct, there is a gradual increase in the

in table 1. All the joints of the successfully sterilized, the unsuccessful-fully sterilized and the control groups are listed according to the amount of motion and swelling, with an average of each group. In figure 1, there is a comparison of the amount of motion in each group over a period of thirty days. In figure 2, there is a comparison of the amount of motion in each of the four gentian groups of the sterilized joints over a period of thirty days.

### ROENTGENOLOGIC STUDY

In taking the roentgenograms attempts were made to follow the clinical changes of the joints in the different stages of activity. From

TABLE 1—Degree of Clinical Activity in All Joints Manifested by Limitation of Motion and Swelling

Limit of motion		0		1-10°		10-40°		60°-90°		90°-135°		Average		Total joints	
1 Successfully sterilized		1		1		1		2		3		57		6	
(a) 0.2% aqueous gentian		(1) Limit of motion		(2) Swelling		(1) Limit of motion		(2) Swelling		(1) Limit of motion		(2) Swelling		(1) Limit of motion	
(b) 0.25% dextrose gentian		1		1		1		1		2		57		3	
(c) 0.5% dextrose gentian		1		1		1		1		2		57		1	
(d) 0.5% olive oil gentian		3		1		1		1		2		57		4	
(1) Limit of motion		(2) Swelling		(1) Limit of motion		(2) Swelling		(1) Limit of motion		(2) Swelling		(1) Limit of motion		(2) Swelling	
2 Unsuccessfully sterilized		3		4		2		3		2		137°		3	
(1) Limit of motion		(2) Swelling		(1) Limit of motion		(2) Swelling		(1) Limit of motion		(2) Swelling		(1) Limit of motion		(2) Swelling	
3 Control		1		1		1		1		2		137°		4	
(a) Staphylococcus aureus		(1) Limit of motion		(2) Swelling		(1) Limit of motion		(2) Swelling		(1) Limit of motion		(2) Swelling		(1) Limit of motion	
(b) Gentian Violet		4		4		4		1		4		117°		4	
(1) Limit of motion		(2) Swelling		(1) Limit of motion		(2) Swelling		(1) Limit of motion		(2) Swelling		(1) Limit of motion		(2) Swelling	
4		4		4		4		4		4		4		4	
5		4		4		4		4		4		4		4	
6		4		4		4		4		4		4		4	
7		4		4		4		4		4		4		4	
8		4		4		4		4		4		4		4	
9		4		4		4		4		4		4		4	
10		4		4		4		4		4		4		4	
11		4		4		4		4		4		4		4	
12		4		4		4		4		4		4		4	
13		4		4		4		4		4		4		4	
14		4		4		4		4		4		4		4	
15		4		4		4		4		4		4		4	
16		4		4		4		4		4		4		4	
17		4		4		4		4		4		4		4	
18		4		4		4		4		4		4		4	
19		4		4		4		4		4		4		4	
20		4		4		4		4		4		4		4	
21		4		4		4		4		4		4		4	
22		4		4		4		4		4		4		4	
23		4		4		4		4		4		4		4	
24		4		4		4		4		4		4		4	
25		4		4		4		4		4		4		4	
26		4		4		4		4		4		4		4	
27		4		4		4		4		4		4		4	

one to five roentgenograms were made of every joint after the infection. Only the final roentgenogram in each joint is described here.

1 Successfully Sterilized—(a) and (b) 0.25 Per Cent Aqueous and 0.25 Per Cent Dextrose Gentian. One animal showed a slight clouding, one showed irregular joint surfaces, two showed destruction of the bone on the opposing surfaces of the tibia, femur and patella and five showed all of the foregoing changes, in addition to changes in the tibia and femur proper, such as thinning of the lower end of the femur and thickening of the upper end of the tibia.

(c) 0.5 Per Cent Dextrose Gentian. A slight clouding of the joint spaces was seen without changes in the bone.

(d) 0.5 Per Cent Olive Oil Gentian. One animal showed irregular changes in the bone on the joint surfaces, and three showed changes in the lower end of the femur and upper end of the tibia.

diameter of the channel toward the duodenum. This increase reaches maximal proportions at the site of confluence with the hepatic ducts of the left lobe of the liver, from which point there is a gradual reduction in the circular dimensions of the common duct until it reaches the duodenum. This increase is largely due to an abundance of muscle fibers, both longitudinal and circular, which extend throughout the entire length of the common duct. In the upper portion of the common duct, the muscle and the layers of connective tissue are of equal width.



Fig 9—A cross-section of the intraduodenal portion of the common bile duct, wide band of muscle fibers and narrow zone of connective tissue may be noted,  $\times 127$

while nearer the duodenum there is a progressive increase in the amount of muscle tissue and a decrease in the extent of the layer of connective tissue. In the lower part of the common duct, the layer of muscle is twice as thick as that of the connective tissue. Circular muscle fibers are more abundant but external to these, and in more or less restricted areas, there are scattered muscle bundles running longitudinally and diagonally (fig 8). Continuing intraduodenally, the



2 *Unsuccessfully Sterilized*—All these animals showed a large amount of bone destruction on the joint surfaces, and changes in the tibia and femur proper changes as in the unsuccessfully sterilized group

3 *Controls*—(a) *Staphylococcus aureus* All showed essentially the same changes as in the unsuccessfully sterilized group

(b) Gentian Violet No changes were noted in the joint surfaces or spaces

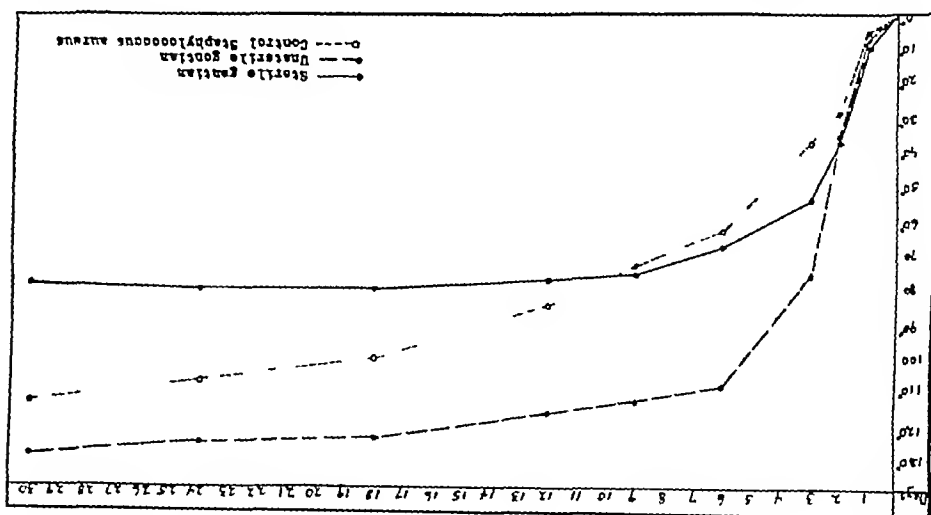


Fig 1—Clinical reaction in degrees of limitation of extension of the successfully sterilized, the unsuccessfully sterilized and the control joints infected with *Staphylococcus aureus* over a period of thirty days

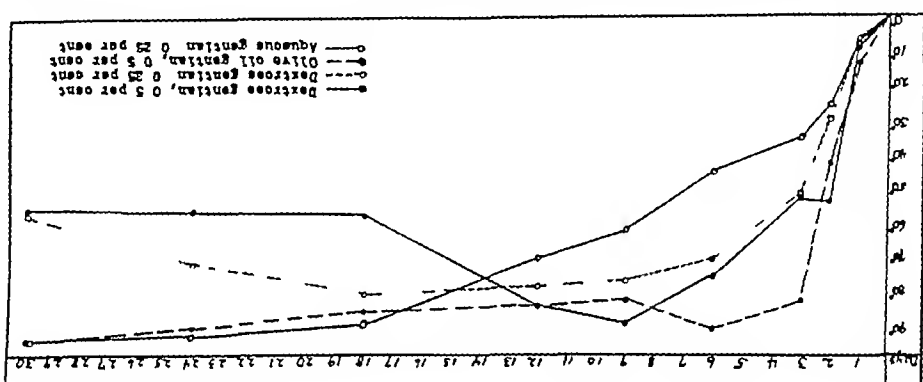


Fig 2—Clinical reaction in degrees of limitation of extension of the successfully sterilized joints in the group in which 0.5 per cent devtrose, 0.25 per cent devtrose, 0.5 per cent olive oil and 0.25 per cent aqueous gentian were used over a period of thirty days. The reaction was markedly less in the groups in which devtrose and gentian were used

#### GROSS PATHOLOGIC STUDY

Eighteen of the twenty-seven joints were examined and the appearance of the joint structures was noted

1 *Successfully Sterilized*—(a) and (b) 0.25 Per Cent Aqueous and Devtrose Gentian Seven of the nine joints in these groups were opened. Four showed a marked bone destruction of the surfaces of the femur, tibia and patella. Three

preponderance of muscle tissue is even greater, and the connective tissue is restricted to a narrow zone immediately around the mucosa.

The bullhead differs from many higher vertebrates in that the common duct passes directly through the duodenal wall into the lumen of the intestine, opening by a single orifice. The muscle of the common duct continues throughout the entire intramural course and there is an appreciable increase in the volume of this tissue within the duodenal wall. Whether this should be designated a sphincter of Oddi is questioned, it is but a continuation of the extensive musculature of the extraduodenal common duct and is not abruptly increased on entering the wall of the intestinal tract. A layer of muscle, however, entirely independent of the muscularis of the duodenum and approximately equal to it in thickness, surrounds the intramural portion of the common duct and is probably highly contractile during the evacuation of the biliary tract such as occurs following the meal of fat (fig. 9).

#### COMMENT

These observations on the contraction of the extrahepatic biliary tract in the common bullhead following a meal rich in fats are interesting because of the facts disclosed pertinent to the manner in which the bile in the gallbladder is discharged. In studies hitherto reported various conflicting interpretations of the mechanism of emptying the gallbladder have been advanced. Observations have been made on mammals, particularly on the cat and the dog, and anesthesia or extensive preliminary surgical procedures may have complicated the ensuing normal physiologic processes. These particular factors are probably obviated in the selection of the fish as a fit subject for such observations. It is not likely that the careful confinement of such an animal for any given length of time will essentially modify the physiologic responses of the body, nor is it likely that psychologic function would be so disturbed as seriously to impair the normal nervous activity accompanying the gastro-intestinal response to diet. Thus it would seem that in the fish one may observe the processes that obtain in a normal biliary tract uninterrupted or unmodified by the nervous reactions set up in more highly organized animals under essentially experimental conditions.

Obviously caution must be used in applying conclusions of observations made on a fish to the highly organized animal. It is probably true that in the modification of structure pursuant to specialization, differentiation in the physiologic response may have arisen, and yet with the present status and limitations of study one cannot be at all certain that contractile processes so clearly shown in the biliary tract of fishes may not be true for higher animals as well. The anatomic organization of the tracts in the various animals studied is essentially the same.

showed a severe fibrous tissue reaction in the joint proper. In six, nodules of cheesy, caseous material were seen about the joints. Pus was found in the joints of three, gentian in the joints of two and gentian in the surrounding tissues of five.

(c) 0.5 Per Cent Dextrose Gentian. Two of the four in this group were examined. One showed a rather large amount of gentian in the joint proper and in the surrounding tissues, without changes in the joint or pus. This was

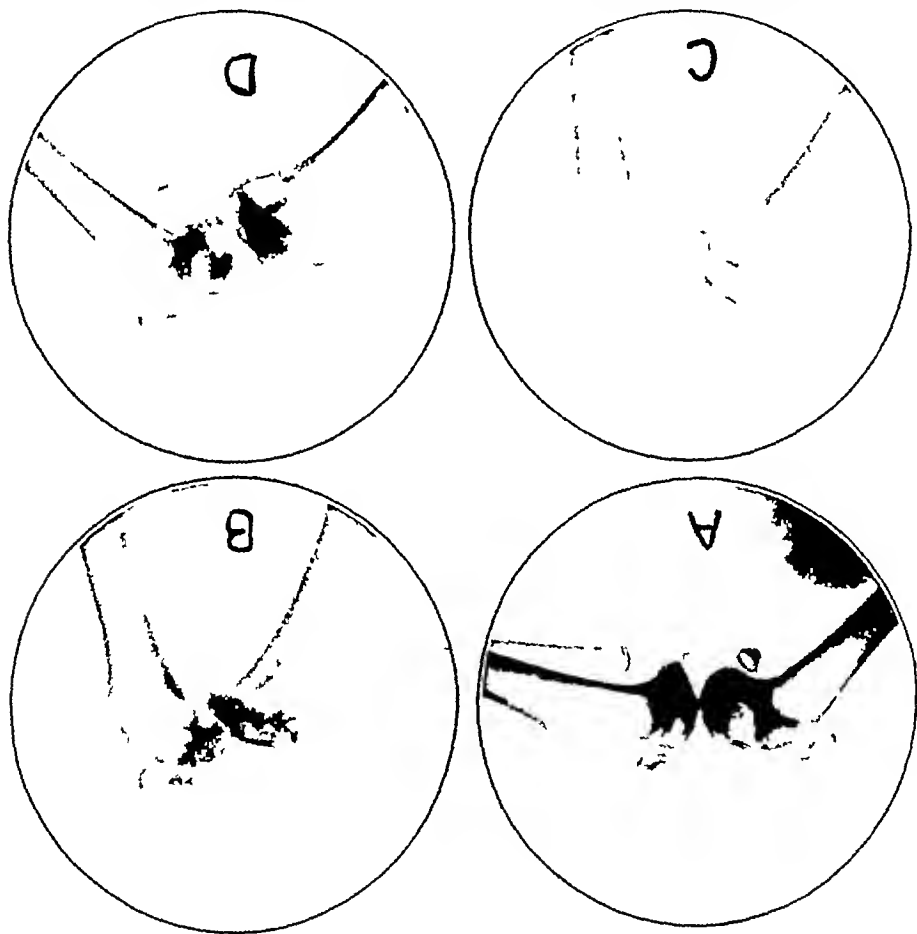


Fig. 3—Early roentgen-ray changes in a successfully sterilized, an unsuccessfully sterilized and a control joint infected with *Staphylococcus aureus*. A indicates a normal joint, B, sterile joint of rabbit 28 on ninth day—0.5 per cent dextrose gentian injected, C, unsterile joint of rabbit 23 on eighth day—0.25 per cent dextrose gentian injected, D, control joint of rabbit 1 infected with *Staphylococcus aureus* on tenth day. The following points should be noted: (1) the clouding of joints B, C and D, compared with the normal joint A, and (2) the irregularity along the under surface of the patella, the anterior border of the femur and the posterior portion of the tibia in the control joint D, which is not seen in B and C.

on the twenty-first day after infection. The other joint was opened five and one-half months after infection. It presented an entirely different picture. There was a marked erosion of all cartilage with bits of cartilage in the joint. The

All observers agree that the biliary tracts of fishes and other animals are composed of serosa, muscle tunic of varying proportions connective tissue sheath and mucosa of columnar epithelium. Differences may abound in the relative abundance of the various tissues involved or in peculiar modifications of certain of the tissues to form additional structures such as the valves of Heister, gland of Lushka or parietal sacculi, but the essential groundwork in the structural organization of these extrahepatic biliary tracts is identical. There is some basis for assuming, then, that there may be unity in the physiologic responses of these biliary tracts although phylogenetically so remote.

It is not my purpose here to attempt a correlation of fishes and other animals, or to attempt any explanation of the phenomena known to occur in the biliary tracts of mammals with facts observed in the fish. But rather, I wish further to substantiate certain conclusions hitherto reached from studies on the dog and the guinea-pig and to show that the lowly fish possesses an hepatic organization which responds to fat in a manner compatible with previously recorded data on the emptying of the gallbladder.

Gathered from the available sources of published data on the emptying of the gallbladder, various factors have been accorded some influence on the discharge of bile from the gallbladder. Chief among these are intra-abdominal pressure, secretory pressure of the liver, peristalsis of the duodenum together with duodenal tone and contraction of the muscle layer within the wall of the gallbladder. Certain of these factors have been stressed to the entire elimination of the others, but perhaps more recently the preponderance of data favors contraction.

In the light of recent observations, adequate data are presented to throw considerable doubt on the validity of certain of the foregoing factors. First, the animal under experiment is opened by a median abdominal incision so that a major portion of the viscera including the bile tract is exposed during the entire period. Extraneous pressure of any sort is thereby obviated, and the evidence points conclusively to the fact that intra-abdominal pressure or any other form of "squeeze" is not a factor in the discharge of bile from the gallbladder.

During the earlier part of the experiment, soon after the introduction of the fat in the duodenum, hepatic bile passes through the bile duct into the duodenum. This continues to flow for some time, and yet there is not the slightest evidence that the bile in the gallbladder is discharged into the common duct at any time during these early stages of the experiment.

When the abdominal cavity is opened, the entire gastro-intestinal tract is in a state of rest. The tract, being devoid of food for some time, is empty and the walls are collapsed. Immediately on the injection of 2 cc. of egg-yolk and cream into the duodenum, the tract comes

crucial ligaments were relaxed, and they allowed an abnormal amount of lateral mobility. A slight fibrous tissue proliferation was present on the sides of the joint.

(d) 0.5 Per Cent Olive Oil Gentian. Two of the four joints in this group were opened. These showed pus in the joint, and pus and gentian in the surrounding tissues. There was a roughening of the articular cartilage in both, with a thinning of the crucial ligaments and semilunar cartilages in one. The lower end of the femur in one showed a nodular swelling.

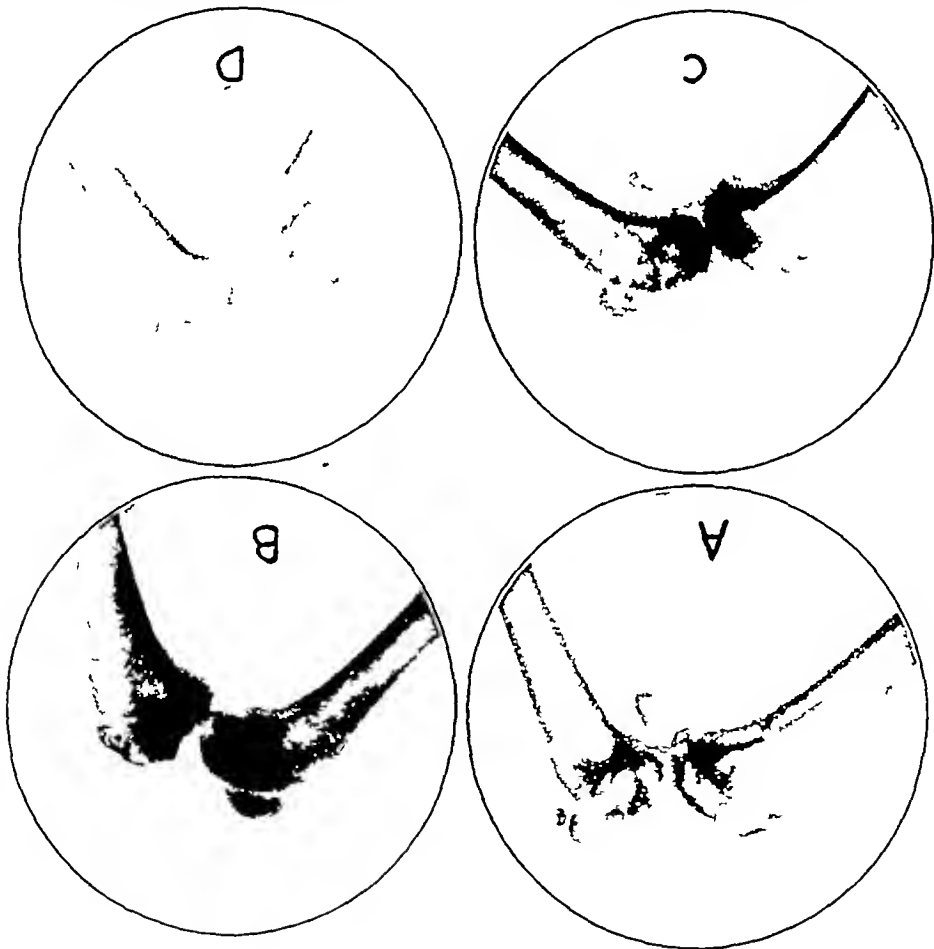


Fig 4—Later roentgen-ray changes in two successfully sterilized joints and one unsuccessfully sterilized joint, compared with a control joint in which gentian was used. *A* indicates a control joint, injected with gentian, from rabbit 15 on the thirty-second day—0.25 per cent dextrose injected, *B*, sterile joint from rabbit 26 on twenty-seventh day—0.5 per cent olive oil gentian injected, *C*, sterile joint of rabbit 21 on thirty-second day—0.25 per cent dextrose gentian injected, *D*, unsterile joint of rabbit 14 on thirty-second day—0.25 per cent dextrose gentian injected. The following points should be noted: (1) the complete absence of changes in the control joint *A*, in which gentian was used, (2) the marked irregularity and bone destruction in *B*, *C* and *D*, and (3) the areas of absorption in *D*.

2 *Unsuccessfully Sterilized*—One of the three in this group was opened. This showed pus in the joint and tissues, gentian in the tissues, a marked fibrous tissue proliferation in the joint and a roughening of all bony surfaces.

into tone, the muscles contract and peristalsis becomes active. Anti-peristalsis of the duodenal region is especially characteristic. The stomach, although without the food as a stimulating factor, becomes contractile. These peristaltic waves of varying lengths and force which pass repeatedly over the orifice of the common bile duct do not appear to have any effect on the flow of bile. The gallbladder remains entirely inactive throughout the entire period that the duodenum is motile. The common duct, too, is inactive so far as movement is concerned during this interval. The conclusion is obvious then, that peristalsis or muscle tone of the duodenum does not have any effect on the discharge of bile in this animal.

This entire study adequately supports the observation, now generally accepted, that bile is discharged from the gallbladder by the active contraction of an intrinsic musculature. The common duct is also shown to be contractile, aiding thereby the evacuation of the gallbladder. Extrahepatic biliary motility is not apparent until from an hour to an hour and a half after the injection of fat into the duodenum. This motility expresses itself in the form of contraction waves that arise in the upper part of the hepatic tract and travel toward the duodenum in one direction and back over the gallbladder in the other direction. These waves are not interrelated, for one may arise without the other. Usually a wave that arises at the customary site, to course toward the duodenum will pass throughout the common duct, while waves passing over the gallbladder are frequently incomplete. While the gallbladder is in a state of contraction, waves may arise at the fundus and pass partially or completely over it, as well as in the reverse direction.

The time interval before the contraction of the gallbladder following the introduction of the fat suggests that the causal factors involved in this motility are in some way related to absorption. The independent vascular connection of the duodenum with the gallbladder and the cystic duct is suggestive, and studies are now under way to determine, if possible, the absorptive route and the factors underlying the contraction of these biliary channels.

#### SUMMARY

The gross and microscopic anatomy and the motor activity of the extrahepatic biliary tract in the common bullhead are reported. In this animal, the gallbladder hangs relatively free from the liver and may readily be exposed by slight traction on the duodenum, so that continuous observations on the emptying of the gallbladder in response to a meal of fat are readily made. A method is described for properly aerating the animal and exposing the viscera preparatory to such continuous observation.

3 Controls—(a) *Staphylococcus aureus* Three of the four joints in this group were opened. Two showed pus in the joint, a large fibrous tissue reaction in the joint and a roughening of all bony surfaces. One was opened seven months after the infection. This showed a large amount of fibrous tissue in the joint with evidence of new bone formation. All the cartilage had been destroyed. Trunk pus was not encountered.

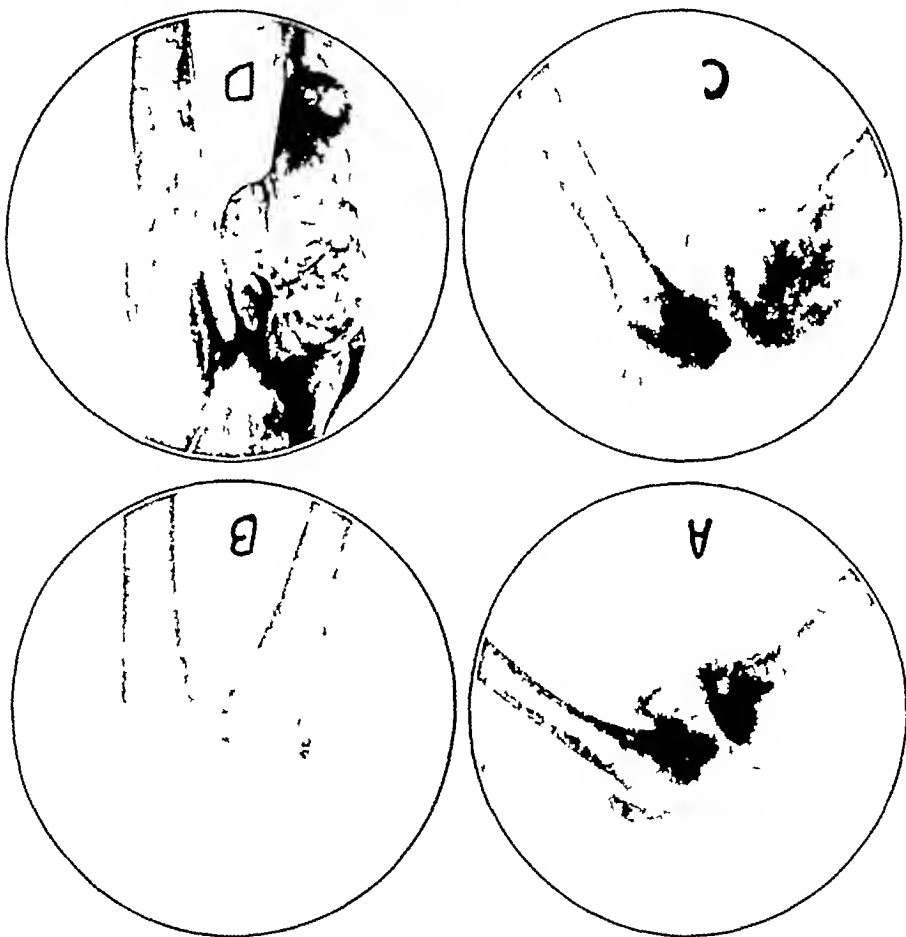


Fig. 5—Most marked roentgen-ray changes in a successfully sterilized, an unsuccessfully sterilized and a control joint infected with *Staphylococcus aureus*, and the extra-articular caseous nodules found in many of the infected joints. A indicates a sterile joint of rabbit 5 on the eighty-sixth day—0.25 per cent aqueous gentian injected, B, unsterile joint of rabbit 10 on seventy-sixth day—0.25 per cent aqueous gentian injected, C, control joint of rabbit 1 infected with *Staphylococcus aureus*, on thirty-seventh day, D extra-articular caseous nodules in rabbit 1 on thirty-seventh day. The following points should be noted (1) the clouding, irregularity and bone destruction in A, B and C, (2) the areas of absorption in B, and (3) the thinning of the lower end of the femur and thickening of the upper end of the tibia in C.

(b) Gentian Violet These three were opened and found to have a small amount of gentian in the surrounding tissues. Changes had not occurred in the joints.

Following the intraduodenal injection of a few cubic centimeters of egg-yolk and cream, active peristalsis and antiperistalsis of the gastro-intestinal tract are induced. Hepatic bile is discharged into the duodenum, but the gallbladder remains inactive during the period of gastro-intestinal activity.

Within periods of time varying from an hour and fifteen minutes to an hour and forty-five minutes, muscle tonus over the gallbladder is apparent. Contraction waves soon pass over the vesicle and force out portions of the contained bile into the common bile duct. These waves originate within the upper portion of the bile duct near its continuity with the gallbladder and pass in a reverse direction over it. Likewise, contraction waves pass over the entire common bile duct and force the contained bile into the duodenum. Subsequently, contraction waves arise at the fundus of the gallbladder and pass over the vesicle to the bile duct. Waves of the common duct and waves of the gallbladder tunic are not necessarily synchronous.

There is conclusive evidence that (1) the gallbladder in the common bullhead empties by the contraction of the muscle tunic within its wall, (2) the emptying of the gallbladder is related to the extent of gastro-intestinal absorption of fat, (3) intra-abdominal pressure is not a factor in the discharge of bile from the gallbladder, and (4) duodenal peristalsis or duodenal muscle tone is entirely ineffectual in the discharge of bile from the gallbladder.



## MICROSCOPIC PATHOLOGIC STUDY

The data for the microscopic pathologic study is based on the sections of nineteen out of the twenty-seven joints. Only the general results will be given.

1 *Successfully Sterilized*—(a) and (b) 0.25 Per cent Aqueous and Dextrose Gentian. Six of the nine joints were studied. Pus was found in the joints of five and in the tissues of three. In one there were three abscesses in the epiphysis of the tibia. The cartilage was eroded on the surface of the tibia in all and on the femur in all except one. In one the cartilage was found in the joint. In one, the cartilage showed a proliferation, while in another one the fibrous tissue was replacing the cartilage. There was a moderate fibrous tissue reaction in the joints of four. In one there was a definite increase of the fibrous tissue in the popliteal space. In four the bone marrow in the epiphysis was supplanted by fibrous tissue. In one there was a heavy fibrous band across the joint. The crucial ligaments and patella were normal in two. In one spicules of bone were present in the joint, with bony projections into the joint not covered by cartilage or fibrous tissue. Gentian was found in the joint of one and in the surrounding tissues of three.

(c) 0.5 Per cent Dextrose Gentian. One of the four was studied. This was five and one-half months after the infection. Pus was found in the tissues. There was an erosion of cartilage on all the joint surfaces with sequestration into the joint. Parts of the joint showed bony spicules projecting into the joint space, completely denuded of cartilage. There was evidence of cartilage proliferation. A large amount of fibrous tissue was present in the joint with an increase in the popliteal space. The crucial ligaments were thinned. The reaction showed healing.

(d) 0.5 Per cent Olive Oil Gentian. All four joints were studied. The joint reaction was more marked here than in any other group. Pus was present in the joints of three and in the surrounding tissues of one. There was an abscess in the femur of one. The cartilage of both the femur and tibia was eroded in all four with a sequestration of small bits into the joint. In one spicules of bone were present in the joint. In two the cartilage on the anterior surface of the femur was not eroded. A marked fibrous tissue proliferation was seen in all. In three fibrous tissue replaced cartilage, while in all four the bone marrow of the epiphyses was replaced with fibrous tissue. The posterior part of the capsule and crucial ligaments were thicker than normal in one.

2 *Unsuccessfully Sterilized*—Two of the three were studied. A large amount of pus was found in the joints and tissues. Abscesses were present in the bone, one showing the femur and tibia involved and the other, only the tibia. One showed a large collection of pus beneath the periosteum on the anterior border of both the femur and the tibia. The cartilage was eroded over all the joint surfaces, and had sequestered into the joint. A marked fibrous tissue proliferation was present through the joints. In one cartilage was replaced by fibrous tissue, while in another the bone marrow was supplanted by fibrous tissue.

3 *Controls*—(a) *Staphylococcus aureus*. Three of the four were studied. One of these showed only a moderate reaction while the other two showed the most marked reaction in the series. The first showed a slight amount of pus and

# PYOGENIC ARTHRITIS IN THE KNEE JOINT OF RABBITS

## TREATMENT WITH GENTIAN VIOLET EXPERIMENTAL STUDY \*

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One of the frequently discussed problems of the present day is the use of gentian violet and mercurochrome in the treatment of disease and infection. The type of infection treated has not been limited to one group of cases. The exact nature of the reaction of these drugs in combating infection has not been satisfactorily explained. With this thought in mind, a study has been made of the reaction of gentian violet in joints infected with *Staphylococcus aureus*. This study has involved a careful investigation of this type of arthritis, and it is hoped that some light may be thrown on arthritis in general.

Churchman has published three articles on the treatment of infections of the joint with gentian violet. First, in 1915 he<sup>1</sup> demonstrated an apparatus for the irrigation of a joint, followed by an instillation of gentian violet. He felt that in joints with a purulent infection the synovial membrane should be cleared of the film of pus and necrotic tissue present before the instillation of the gentian violet. The gentian violet in a 1 to 10,000 solution could then penetrate the synovial membrane to destroy the organisms. In 1918, he<sup>2</sup> reported the perfected apparatus for joint lavage, and eight cases, in two of which successful results were obtained in pyogenic joints. In 1921, he<sup>3</sup> reported six cases, in two of which good results were obtained in staphylococcus infections. In 1924, Churchman<sup>4</sup> stated that the most striking characteristic of gentian violet was its bacteriostatic power, in addition to its bactericidal power. Its great value lay in its penetration into tissues, which is impossible for antiseptics not in the triphenyl methane group of dyes. He showed that in a human knee the dye stained the nucleus and protoplasm of the endothelial cells and penetrated to the underlying connective tissue, but did not injure the synovial membrane. He showed this in an infected joint treated first with lavage.

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\* From the Louise Bowles Foundation of the Children's Hospital School, Baltimore.

1 Churchman, J. W. Ann Surg **62** 409, 1915

2 Churchman, J. W. Treatment of Acute Infections of Joint, J. A. M. A **70** 1047 (April 13) 1918

3 Churchman, J. W. Gentian Violet in Treatment of Purulent Arthritis, J. A. M. A **75** 583 (Aug. 28) 1921

4 Churchman, J. W. J. Urol **11** 1, 1924

erosion of cartilage, while the only evidence of fibrous reaction was a band across the joint. The latter two showed a large amount of pus in the joints with a slight amount in the tissues. Two large abscesses were seen in the tibia of one. There was marked cartilage erosion with sequestration into the joint. One showed spicules of bone in the joint. The fibrous tissue in the joint was marked. In one a heavy fibrous band ran across the joint. In both bone marrow was replaced with fibrous tissue.

(b) Gentian Violet. Little reaction was noted in the three. All showed an infiltration of leukocytes into the joint, and two showed a small amount of gentian. In the surrounding tissues of one gentian was found, and in another, an infiltration of leukocytes.

In summarizing the microscopic pathology four groups of changes have been noted

- (1) Acute inflammatory changes, such as pus and necrotic tissue in the joint and in the periauticular tissues, abscess formation around the joint, in the joint and in the bone proper, and pus beneath the periosteum of the bone
- (2) Cartilaginous changes, such as erosion, destruction and sequestration into the joint, and proliferation
- (3) Bony changes, such as spicules of bone projecting into the joint, and sequestration
- (4) Fibrous tissue changes, such as extreme proliferation through the joint, bands across the joint, a thickening of the popliteal tissues and a replacement of cartilage and bone marrow with fibrous tissue

#### COMMENT

In the bacteriologic study of the successfully sterilized joints, the group in which 0.5 per cent dextrose gentian was used was sterilized the most quickly, the average time being three days. In two of the four joints, the cultures were sterile in twenty-four hours after the injection of the gentian violet. An explanation of this is that the injections of the gentian followed promptly after the infection, and that 4 per cent dextrose as a medium is more efficient than water or olive oil. In the joints in which 0.25 per cent dextrose gentian was used, the average time of sterilization was thirteen days. In these the injection of gentian did not follow the infection as promptly as in the joints in which 0.5 per cent dextrose gentian was used. In the joints treated with 0.25 per cent aqueous gentian, the average time of sterilization was twenty-one days. Again the gentian was not given as promptly after the infection and the medium for the gentian was not felt to be as efficient as 4 per cent dextrose. When 0.5 per cent olive oil gentian was used, the average time of sterilization was twenty-two days. With this group the gentian was injected promptly after the infection, but the varying factor was the medium. The aspirations showed that the olive oil gentian remained in the joints longer than in the other sterile groups,



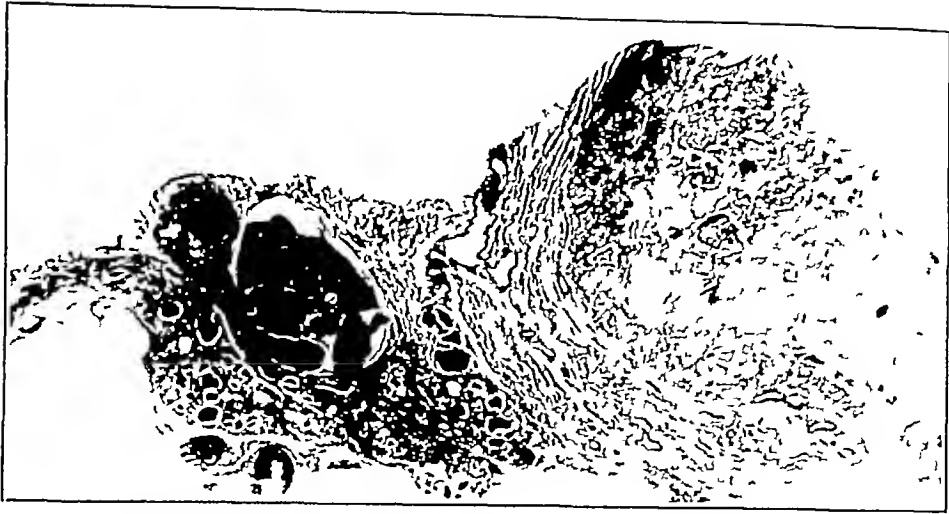


Fig 20—Cross-section of lobe of thyroid gland from patient, aged 60, operated on for nodular goiter with hyperthyroidism. In the right half of the section can be seen a large area of pin staining material surrounded by a rim of hyperplastic thyroid parenchyma. It is apparently encapsulated, but it is seen that the apparent capsule is composed of compressed normal thyroid tissue intervening between the interlobular and intralobular septums. The center of the tumor mass on the right side is made up of fibrous tissue and colloid-like material in which fragments of disintegrated acini can be seen. The nodules to the left are localized apparently encapsulated areas of dilated colloid containing acini. In this picture on the left side one has a typical area of hyperinvolution and on the right side one has a nodule hypertrophy and hyperplasia of the remaining intact parenchyma together with the central degeneration characteristic of involution, the two processes running hand in hand. Reduced from a magnification of  $\times 4$ .

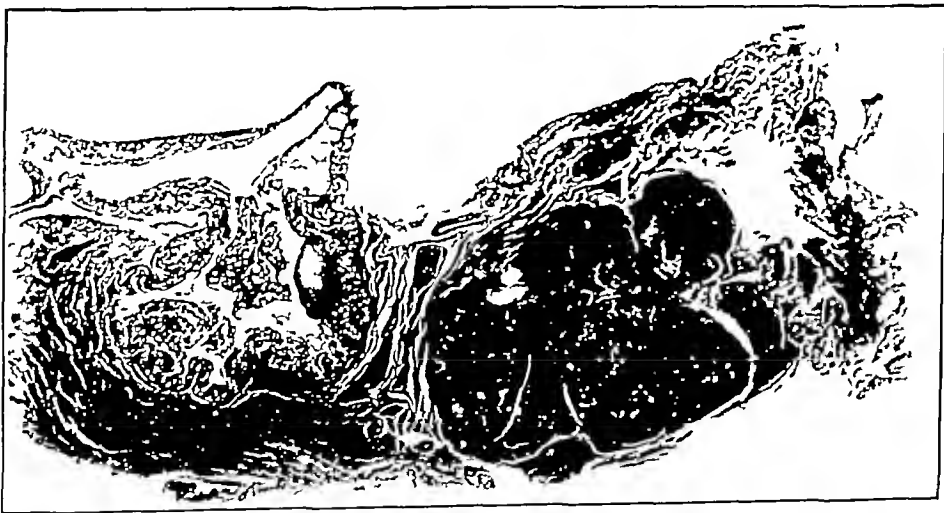


Fig 21—Cross-section of lobe of thyroid tissue from case of nodular goiter with hyperthyroidism showing two localized and sharply defined areas or nodules in which there is hypertrophy and hyperplasia of the epithelium associated with involutional changes. The normal thyroid parenchyma is displaced and compressed between the nodules appearing to form a capsule. The disease process here is localized to these areas. Reduced from a magnification of  $\times 5$ .

so that it must be assumed that the amount of gentian necessary to combat the infection quickly was not available

In the clinical study of the successfully sterilized joints, the group treated with 0.5 per cent dextrose again stands out as the best in the series. The average limitation of extension was 57 degrees and the average amount of swelling a little less than fair. When 0.25 per cent dextrose was used the average limitation of extension was 85 degrees, and the average amount of swelling slightly more than fair. One joint in this group showed only a slight reaction, with 10 degrees' limitation of extension. The 0.25 per cent aqueous method gave an 87 degree limitation of extension with the amount of swelling being fair, while the 0.5 per cent olive oil method gave the same 87 degree limitation of extension with the swelling slightly more than fair. In the gentian controls, there was an average limitation of extension of 7 degrees. In a separate experiment in which guinea-pigs were used, it was shown that there was a definite limitation of motion and proliferation of fibrous tissue after the injection of gentian violet in strengths of 1 to 200 (0.5 per cent), 1 to 100 (1 per cent) and 1 to 50 (2 per cent). In the unsuccessfully sterilized group, there was an average limitation of extension of 127 degrees with an average amount of swelling of slightly more than moderate, while the *Staphylococcus aureus* controls showed an average of 117 degrees' limitation of extension, with a moderate amount of swelling. The difference in motion and swelling in these groups may have been within the limits of variation, however, the greater reaction in the unsuccessfully sterilized joints may have been accounted for by the reaction of the gentian violet on the joint structures, in addition to the reaction of the infection.

The roentgen-ray changes in the joints in which 0.5 per cent dextrose was used were negligible, there being only a slight clouding of the joint. The changes after the 0.25 per cent aqueous treatment and after the 0.25 per cent dextrose treatment were striking, but less marked after the latter. The largest amount of bone destruction was found in the joints in which 0.5 per cent olive oil was used. This group took the longest time for sterilization, hence, there was a greater opportunity for the infection to create the bone changes. The unsuccessfully sterilized joints and the *Staphylococcus aureus* controls showed the same amount of bone destruction as the sterilized joints in which 0.5 per cent olive oil gentian was used. The gentian controls did not show roentgen-ray changes.

The gross pathologic changes corresponded closely to the clinical and roentgen-ray observations. In general, those joints which showed marked bone destruction in the roentgenograms and clinically extreme limitation of motion were found to have acute inflammatory changes, a marked fibrous tissue reaction and both cartilage and bone erosion.

tion of the patella. There was a marked destruction of all cartilage with a roughening of the bone. A small depression was seen in the intercondylar space. Gentian tinted caseous material was found in the popliteal space extending up toward the joint.

Microscopic examination of a poor section of the right knee disclosed the following. Joint outlines could not be determined. There was an infiltration of pus with an engorgement of the vessels in the muscles. There was one large abscess fairly well encapsulated.

RABBIT 11—Sex, female, weight, 2 pounds, 10 ounces (1.25 Kg), age, 4 months. Injection of right knee with 0.1 cc of a twenty-four hour broth culture of *Staphylococcus aureus* on Jan 21, 1926.

Day 1. Right knee showed moderate amount of swelling, with increase in local heat and 20 degrees' limit to extension.

Day 6. Joint showed slight tenderness, increase in local heat and 75 degrees' limit to extension, with tenderness. Culture from joint positive.

Day 9. Joint showed a definite increase in the amount of local heat with about same swelling and slightly less motion.

Day 28. Knee showed tumor swelling on outer lower quadrant, with tenderness marked. The rabbit squealed on manipulation of the joint. Motion not beyond 110 degrees' extension. Weight, 2 pounds, 7 ounces (1.1 Kg). Culture from joint positive.

Day 36. Knee showed marked nodular swelling, especially over the outer lower quadrant, extending down the leg. Motion was limited to 120 degrees. There was an increase in local heat and tenderness. Weight, 2 pounds, 9 ounces (1.2 Kg). Roentgenogram showed a marked destruction about the joint, with a thinning of the condyles of the femur and thickening of the upper end of the tibia, also roughening of the under surface of the patella with small loose pieces of bone in the popliteal space.

Day 42 (autopsy). Culture from joint positive.

There were small nodular masses on the outer side of the right knee. There was a contracture of the knee to 90 degrees and of the hip to the same, with contraction of both the hamstrings and the quadriceps. The right knee was now opened across the patellar tendon. The cartilage was denuded over all the condyles, with a roughening of the bone. Creamy pus was present in a trabeculated sac in the joint, with much fibrous tissue and new bone formation in the joint.

Microscopic examination of a fair section of the right knee revealed the following. There was a slight amount of fibrin and pus in the joint. The crucial ligament stood out clearly and seemed thickened. There was a slight erosion of the cartilage of the tibia, that of the femur seemed almost normal. The patella was intact. There were several loose pieces of bone in the joint. The joint was marked by the absence of a fibrous reaction. The inflammatory process was in the stage of healing.

RABBIT 12—Sex, male, weight, 3 pounds (1.4 Kg), age, 4 months. Injection of right knee with 0.1 cc of a twenty-four hour broth culture of *Staphylococcus aureus* on Jan 21, 1926.

Day 1. There was a slight swelling with no tenderness, increase in local heat or limitation of motion in the knee.

Day 6. The right knee showed a slight amount of swelling, with limitation of 45 degrees' extension. Culture showed heavy growth of organisms.

Day 9. The right knee was more swollen with increase in local heat and limitation of motion.

The one joint opened in the group treated with 0.5 per cent dextrose did not show any disease. This, however, was not typical of this group, for a second joint, sectioned but not opened, showed a moderate erosion of cartilage and bone.

The microscopic pathologic changes were markedly less in the successfully sterilized joints than in the unsuccessfully sterilized ones. The joints in which 0.5 per cent olive oil was used showed by far the most changes in the sterile joints, there being erosion of cartilage, sequestration of bone and a large proliferation of fibrous tissue. The fibrous tissue proliferation presented one of the most interesting pictures of the microscopic study. This was found through the joints, diffusely scattered and in bands, it had caused a thickening of the capsule, and, in places, both the cartilage and bone marrow were replaced by fibrous tissue. The formation of abscesses in the epiphyses of the tibia and femur was striking. Some of these abscesses apparently started in the joint and eroded through the cartilage into the bone. These were found more often in the tibia than in the femur.

#### SUMMARY

It has been shown experimentally that *Staphylococcus aureus* infections of the knee joints of rabbits can be controlled, in 85 per cent of the cases, with injections of gentian violet into the joints. The knees can be sterilized if the gentian violet is injected promptly and adequately after the onset of the infection. The more quickly the infection is controlled, the less extensive the joint changes. The gentian violet itself causes a certain amount of irritation and reaction in the joints. Four per cent dextrose is found to be a more efficient medium for the gentian violet than sterile water or olive oil. It is not believed that injections of gentian violet alone should be resorted to in the treatment of joints infected with *Staphylococcus aureus*, but that this treatment should supplement proper surgical measures for the eradication of the infection.

#### CONCLUSIONS

1 Gentian violet has a definite effect in allaying infections with *Staphylococcus aureus* in the knee joints of rabbits.

2 Gentian violet, if administered early enough and in sufficient quantities, will sterilize the joints.

#### PROTOCOL OF RABBIT EXPERIMENTS

RABBIT 1—Sex, male, weight, 2 pounds, 7 ounces (1.1 Kg), age, 3 months. Injection of right knee with 0.1 cc of a twenty-four hour broth culture of *Staphylococcus aureus* on Dec 21, 1925. Roentgenograms taken of both knees.

Day 1 Right knee was definitely swollen, with increase in local heat, and slight limitation of motion. There was evidence of tenderness with the right leg held up on walking. Rabbit looked toxic.



Day 28 There was a moderate amount of swelling with 110 degrees' limit to extension, with marked tenderness. The rabbit squealed on manipulation. Culture, no growth.

Day 36 There was now 120 degrees' limit to extension, with swelling about the same. Rabbit walked with the leg drawn up. Weight, 2 pounds, 9 ounces (11 Kg). Roentgenogram showed marked irregularity of joint surfaces, with thinning of the condyles of the femur and thickening of the tibia, roughening on the under surface of the patella and small pieces of bone in the popliteal space. Day 42 (autopsy) Pus was not visible in the tissues and there were no nodules, as in the other control rabbits. The extension of the hip and knee was limited to 90 degrees. When the joint was opened creamy yellow pus with some gelatinous material was found. The cartilage was pretty much destroyed, with roughening of the condyles of the femur. There was fibrous tissue in the joint.

Microscopic examination of a section of the right knee showed a marked irregularity of all joint lines with a rather generalized destruction of the cartilage. Areas on the tibia and femur showed definite bone involvement and destruction. The joint was filled with pus and fibrin, with a large amount of fibrous tissue all through. Bands of fibrous tissue were seen between the femur and tibia. Islands of cartilage cells were found in the fibrous tissue. Abscesses were not made out in the bone. The patella showed an irregularity of the under surface, with evidence of fibrous tissue. Leukocytic infiltration was present through the surrounding tissues. There was a large amount of pus and fibrous tissue in the popliteal space. The bone marrow in places had been supplanted by fibrous tissue. The inflammatory process was still in a fairly acute stage.

Rabbit 13—Sex, female, weight, 3 pounds (14 Kg), age, 3½ months. Injection of right knee with 0.1 cc of a twenty-four hour broth culture of *Staphylococcus aureus* on March 1, 1926.

Day 1 Right knee showed definite increase in local heat, with swelling and 5 degrees' limit to motion. Culture from joint showed good growth. Injection of 1 cc of 0.25 per cent devtrose gentian heated to 55 C (131 F).

Day 4 Right knee showed a large amount of swelling, with increase in local heat and crepitation of the joint. Motion limited to 110 degrees. Culture from joint positive. Aspirated thick purple material. Roentgenogram showed a slight clouding of the joint.

Day 5 Joint showed same amount of swelling, with 120 degrees' limit to full extension. Injection of 1 cc of 0.25 per cent devtrose gentian.

Day 10 Joint showed same reaction. Weight, 2 pounds, 12 ounces (12 Kg). Culture from joint positive.

Day 28 Joint was moderately swollen, with evidence of fibrous reaction about, and limit of 135 degrees' extension. Culture from joint showed growth.

Day 32 The knee showed the same motion and swelling, with an additional soft fluctuant swelling below the knee.

Autopsy Culture from right knee positive.

There were many caseous nodules surrounding the right knee with purulent material softer than that in the ones previously reported. There was a marked contraction of the hamstrings preventing extension beyond 135 degrees. Some gentian was found in the caseous material in the popliteal space. The joint was not opened.

Microscopic examination of a section of the right knee showed clearly the destruction and fibrous tissue reaction in the joint. Several large encapsulated abscesses were seen anterior to the head of the tibia. There was a marked erosion of the cartilage along the anterior and posterior parts of the femur and

Day 2 Joint now showed increase in limitation of motion of approximately 70 degrees Swelling was about the same, with slightly less tenderness and local heat

Day 3 Joint showed about the same reaction Culture from joint positive Aspirated milky turbid fluid Roentgenogram of right knee showed a slight haziness about the posterior part of the tibia

Day 5 Right knee showed an increase in the swelling, with the same amount of motion Swelling had extended down the leg to the midpoint of the ankle Limp was still marked but not as sensitive to the touch Culture from joint showed luxuriant growth

Day 6 Joint showed same motion and swelling

Day 10 There was a marked increase in the swelling which was nodular in character about the joint, with 105 degrees' limitation of motion There was evidence of fluid in the joint, with fluctuancy The rabbit looked quite sick and emaciated Weight, 2 pounds, 4 ounces (1 Kg) Culture from joint positive Roentgenogram showed an irregularity of the tibia and femur with the joint distended and the patella lifted up, showing an irregularity on the inferior surface

Day 11 The swelling about the knee was much more marked, with only 20 degrees of motion possible, there being a limitation of 120 degrees of extension The rabbit looked sicker and more emaciated The left knee now showed a limit of the last 20 degrees of extension Culture from joint positive

Day 22 There was now a nodular swelling down the leg to the ankle joint, as well as that about the joint Motion the same

Day 37 (autopsy) Culture from right knee positive for *Staphylococcus aureus* Roentgenogram of the right knee showed marked destruction of all the joint surfaces with a destruction of the condyles and a few bony projections about these also new bone formation about the head of the tibia

The right knee presented a cauliflower-like appearance, with multiple yellowish abscesses beneath the muscular fascia extending from the upper limit of the quadriceps pouches to the lower third of the tibia The joint could not be extended beyond 135 degrees There was a string of fibrous tissue running from the abdominal wall to the knee, holding it up in flexion The joint was not opened

Microscopic examination could not be performed because the specimens were lost

RABBIT 2—Sex, male, weight, 3 pounds (1.4 Kg), age, 3 months Injection of the right ear vein with 0.1 cc of a twenty-four hour broth culture of *Staphylococcus aureus* on Dec 21, 1925 A small dentist's drill was then used to traumatize the right knee, this being put into the joint and moved around in all directions with the drill revolving Roentgenograms were taken of both knees, they were negative

Day 1 The right knee showed a slight limitation to full extension, with a slight amount of swelling There was no increase in local heat with no limp on walking The rabbit, however, looked quite toxic

Day 2 General condition of the rabbit about the same with no change in the knee

Day 3 The right knee showed a limitation of 10 degrees to full extension No swelling The rabbit was more toxic Roentgenogram of the right knee showed a slight haziness behind the tibia

Day 5 Right knee showed same amount of motion with slight amount of swelling The animal looked more toxic and much less lively

over the top of the tibia. A great deal of fibrous tissue was observed through the joint, in parts of which were nests of cartilage cells. Fibrous tissue had completely replaced the cartilage along the borders of the femur. A large fibrous band was found across the joint at one side. Pus and fibrin were seen all through the joint. The anterior border of the tibia was eroded by an abscess which had arisen in the soft tissue. The fibrous tissue was supplanting the bone marrow in places. The inflammatory process was one which was subsiding.

RABBIT 14—Sex, male, weight, 3 pounds, 8 ounces (1.6 Kg.), age, 3½ months. Injection of right knee with 0.1 cc of a twenty-four-hour broth culture of *Staphylococcus aureus* on March 1, 1926.



Fig 7—High power photomicrograph of section from rabbit 13. Autopsy on thirty-second day after infection. Joint culture positive. Joint received two injections of 0.25 per cent dextrose gentian violet. Margins of cartilage erosion with island of cartilage surrounded by fibrous tissue, fibrous tissue proliferation in the joint space and fibrous tissue replacing the cartilage of the bone marrow.

Day 1. Right knee showed a marked increase in local heat, with some swelling and 5 degrees' limit to full extension. Rabbit seemed fairly toxic. Culture showed good growth. Injection of 1 cc. 0.25 per cent dextrose gentian at 55 C (131 F). Day 4. Joint showed moderate amount of swelling, with 100 degrees' limit to extension, with increase in local heat and crepitation. Culture from joint positive. Roentgenogram showed no changes.

Day 6 Right knee showed slightly more swelling with slightly more limitation to full extension. Otherwise rabbit was the same.

Day 10 Rabbit looked quite emaciated, having lost 15 ounces (0.5 Kg) in ten days, and seemed toxic. There was now an ankylosis of the right knee in about 75 degrees' flexion, with only a slight amount of swelling. The animal squealed when the left knee was touched, there being a slight amount of swelling and a limitation of the last 20 degrees of extension. Culture from right knee positive. Roentgenogram of the right knee showed a clouding behind the tibia and in the supracondylar region in front.

Day 11 The right knee seemed slightly more swollen and fluctuant, but the general condition of the rabbit was the same.

Day 15 (autopsy) The rabbit died after being much more toxic during the preceding two days. Culture from right knee joint positive for *Staphylococcus aureus*. Culture from heart's blood positive for *Staphylococcus aureus*. Roentgenogram of the right knee showed about the same clouding with small shadows in the anterior joint space.

The rabbit was extremely dehydrated. The right knee was ankylosed at an angle of 75 degrees, with no evident swelling. When the joint was opened, the surfaces were found to be dull and covered with a sticky purulent exudate. The joint was not examined closely. Small abscesses were found in the liver, kidneys, chest wall and leg muscles.

Microscopic examination of a section from the right knee revealed a marked irregularity of the opposing joint surfaces with a destruction in spots of the cartilage. Two abscesses were present in the tibia, one in the epiphyseal line proper and the other in the epiphysis. There was a rather marked leukocytic infiltration with necrotic tissue in the joint and surrounding tissues. An abscess was seen in the opposing surface of the femur. This seemed to open into the joint. The cartilage destruction was certainly more marked over the opposing surfaces of the femur and tibia. There was a rather marked accumulation of pus in the popliteal space with a distention of the capsule in this region. This joined the abscess in the femur.

RABBIT 3—Sex, female, weight, 2 pounds, 9 ounces (1.1 Kg), age, 3½ months. Injection of right knee, Dec. 28, 1925, with 0.1 cc of twenty-four hour broth culture of *Staphylococcus aureus*.

Day 1 Right knee showed a small amount of swelling, with 10 degrees' limitation of extension and definite increase in local heat. The joint was aspirated, and a luxuriant growth was obtained. Injection of 1 cc. of 0.25 per cent aqueous gentian violet into right knee. Roentgenogram showed a slight clouding about the condyles.

Day 2 Right knee showed the same amount of swelling and motion.

Day 3 No change. Aspiration of joint showed a positive culture.

Day 4 The right knee showed a fair amount of swelling, and 30 degrees' limitation of full extension. Injection of 1 cc. of 0.25 per cent aqueous gentian

Day 10 Right knee showed same amount of swelling and motion. Aspiration showed a positive culture. Injection of 1 cc. 0.25 per cent aqueous gentian. Roentgenogram showed a clouding about all of the joint lines but no destruction of bone.

Day 21 Right knee showed moderate amount of swelling, with 120 degrees' limitation of extension. Aspiration showed a negative culture. Roentgenogram showed a destruction of the opposing joint surfaces of the tibia, femur and patella, with a marked clouding.

Day 5 Joint showed slightly less motion, about 120 degrees' limitation, with same swelling and increase in local heat. Injection of 1 cc of 0.25 per cent dextrose gentian. Culture from joint did not show growth.

Day 10 Joint showed same changes. Weight 2 pounds, 13 ounces (1.2 Kg.) Culture from joint positive.

Day 28 Right knee showed a surrounding fibrous reaction, with moderate swelling and 135 degrees' limit to motion. Culture from joint positive.

Day 32 Knee showed same swelling and motion. Weight 2 pounds, 10 ounces (1.15 Kg.) Autopsy. Culture from joint positive.

Several caseous nodules tinted with gentian were found about the joint and in the popliteal space. There was a contraction of the hamstrings. A large amount of bony swelling in the joint could be palpated. The joint was not opened.

Microscopic examination of section of the right knee revealed the following. This was another section which showed well the reaction and destruction of



Fig 8—Photomicrograph of section from rabbit 14. Autopsy on thirty-second day after infection. Joint culture positive. Joint received two injections of 0.25 per cent dextrose gentian violet. Four distinct abscesses in epiphysis of femur, an abscess behind the head of the tibia, a necrosis of the posterior portion of the epiphysis of the tibia, pus along the anterior margins of the femur and tibia and pus with necrotic tissue in the joint space. This is the section of roentgenogram D in figure 4.

the joint. Abscesses were seen in the popliteal space and in the epiphysis of both the tibia and femur. Those in the femur were linked together and were about four in number. There was a marked fibrous reaction through the joint with pus and fibrin. A layer of pus was seen along the anterior border of both the femur and the tibia. Small islands of cartilage were embedded in the fibrous tissue and pus. There was a destruction of all the cartilaginous surfaces, but it was more marked on the femur. A small sesamoid bone was found in the popliteal space adjacent to an abscess. The bone marrow was supplanted in places by fibrous tissue. The reaction in the joint was that of a fairly acute inflammation.

Day 23 (autopsy) Culture of right knee was negative. Roentgenogram of right knee showed the same bone destruction as previously reported.

There was about 120 degrees' limitation of full extension, with a moderate amount of swelling. There was an infiltration of gentian beneath the muscle on the outer side of the tibia for almost its whole length. There were many small yellowish areas over the head of the tibia suggesting tiny abscesses in the muscles and fascia. A definite contracture of the hamstrings was found. When the knee joint was opened, a large amount of grumous purplish material was found, with a large amount of fibrous tissue throughout. Some roughening of the bony surface was noted.

Microscopic examination of a section from the right knee revealed remarkably well preserved joint lines, considering the amount of reaction. There was a large amount of fibrous tissue in the joint, with gentian and leukocytes. On the cartilaginous surfaces of the femur and tibia, deposits of leukocytes, fibrin and necrotic tissue were present. The crucial ligaments were preserved and had the same deposits. A rather heavy fibrous band ran through the joint. There was a thinning and destruction of the cartilage in spots. There was one area which suggested a proliferation of cartilage somewhat similar to a chondrosarcoma. A large amount of gentian and necrotic material was found through the muscles. The cartilage was eroded over the popliteal surface of the femur with beginning abscess formation in the femur. There were a few deposits of leukocytes and necrotic material through the adjacent area of the bone marrow.

RABBIT 4—Sex, female, weight, 2 pounds, 12 ounces (12 Kg), age, 3½ months. Injection of right knee with 0.1 cc. of a twenty-four hour broth culture of *Staphylococcus aureus* on Dec. 28, 1926.

Day 1. Right knee showed a slight limit to full extension, with no swelling or increase in local heat. There was a slight limp.

Day 2. Knee showed the same condition. Injection of 1 cc. 0.25 per cent aqueous gentian. Roentgenogram showed a slight clouding and irregularity behind the condyles of the femur.

Day 3. The joint had a slight limitation to full extension, about 15 degrees, with slight swelling. Culture from joint showed good growth.

Day 4. The joint showed the same limitation of motion and swelling.

Day 5 (autopsy). The rabbit died after a severe, acute diarrhea with prostration. Culture from right knee joint positive. Culture from heart's blood showed *Bacillus hofmani*. Roentgenograms of the right knee showed a clouding about the joint, especially of the lower femur.

On examination, the right knee showed about 15 degrees' limitation to full extension, with a fair amount of swelling. When the knee was opened, a large amount of thick creamy pus was found, which extended up into the quadriceps pouches. The joint surfaces were not carefully examined. There was no evidence of abscess in any other part of the body.

Microscopic examination of a section from the right knee revealed a remarkably small amount of reaction in the joint. A fair amount of pus and fibrin was present but there was no fibrous tissue in the joint. The cartilage of the tibia and femur did not show erosion. The patella and semilunar cartilages were intact. The subpatellar fat pad was well shown and there was no reaction. There was a moderate engorgement of vessels and leukocytic infiltration in the surrounding tissues. The inflammatory process was not far enough advanced in this region to be acute.

RABBIT 15—Sex, male, weight, 2 pounds, 15 ounces (1.4 Kg), age, 4 months. Injection of the right knee with 1 cc of 0.25 per cent dextrose gentian violet on March 2, 1926.

Day 1. No reaction could be made out in the knee.

Day 5. There was a slight limitation of extension. No swelling, and no increase in local heat.

Day 32. The right knee showed a slight amount of swelling, with a limitation of the last 10 degrees of extension. Roentgenogram did not show joint changes, but a slight shadow in the popliteal space.

Autopsy. When the skin was removed, the joint had the normal healthy appearance with a gloss to the patellar tendon. When the joint was opened this was essentially normal. There was a slight roughening of the cartilaginous surfaces. All ligaments and other cartilages were normal. A small pocket of gentian was found in the popliteal space. There was about 5 degrees' limitation to extension.

Microscopic examination of the right knee disclosed the following. The cartilage was regular. There was no evidence of any reaction in the joint. A few pus cells and fibrin were present in the joint. The section was only fair.

RABBIT 16—Sex, female, weight, 3 pounds, 9 ounces (1.6 Kg), aged, 3½ months. Injection of the right knee with 0.1 cc of a twenty-four-hour broth culture of *Staphylococcus aureus* on March 5, 1926.

Day 1. Right knee showed a slight amount of swelling, with increase in local heat, and about 5 degrees' limitation to extension. Culture from joint positive. Injection of 1 cc of 0.25 per cent dextrose gentian.

Day 3 (autopsy). Culture from right knee positive. Roentgenogram of the right knee did not show any changes. The rabbit died without any apparent cause, with no evidence of diarrhea or prostration as seen in rabbit 4.

When the joint was removed there remained only the last 10 degrees of extension, limited, with little swelling. A fair amount of the gentian was found in the muscles of the lower thigh in the popliteal space. When the joint was opened a fair amount of the gentian was present, with an exudate resembling inspissated pus. There was no evidence of fibrous tissue reaction in the joint. Synovial membrane seemed eroded over the condyles of the femur and beneath the patella.

A rather generalized congestion of all organs, the liver, kidneys, heart and lungs was found. A greenish stain was present over the right abdominal wall. Microscopic examination of a section from the right knee revealed a little reaction in the joint. A small amount of gentian was present and in the surrounding muscles. A few leukocytes were present in the joint and a great many in the muscles. There was a slight irregularity of the cartilage along the border of the femur. Fibrous tissue was not present in the joint.

RABBIT 17—Sex, male, weight, 3 pounds, 2 ounces (1.45 Kg), age, 3½ months. Injection of right knee, March 5, 1926, with 0.1 cc of a 24 hour broth culture of *Staphylococcus aureus*.

Day 1. Right knee showed a slight amount of swelling, with an increase in local heat and 10 degrees' limitation of extension. Culture from joint positive. Injection of 1 cc of 0.25 dextrose gentian violet.

Day 6. Right knee showed a slight increase in swelling and about the same limitation of motion.

Day 20. There was about 60 degrees' limitation of extension in the knee, with a slight increase in swelling. There was a definite contraction of the hamstring.

RABBIT 5—Sex, male, weight, 2 pounds, 10 ounces (12 Kg), age, 3½ months  
Injection of right knee, Jan 6, 1926, with 0.2 cc of twenty-four hour broth culture of *Staphylococcus aureus*

Day 1 Right knee showed a small amount of swelling, with 10 degrees' limitation of extension and increase in local heat. Joint aspirated but no growth obtained. Injection of 1 cc of 0.25 per cent aqueous gentian violet

Day 2 Right knee showed 90 degrees' limitation of extension, with a fair amount of swelling and increase in local heat

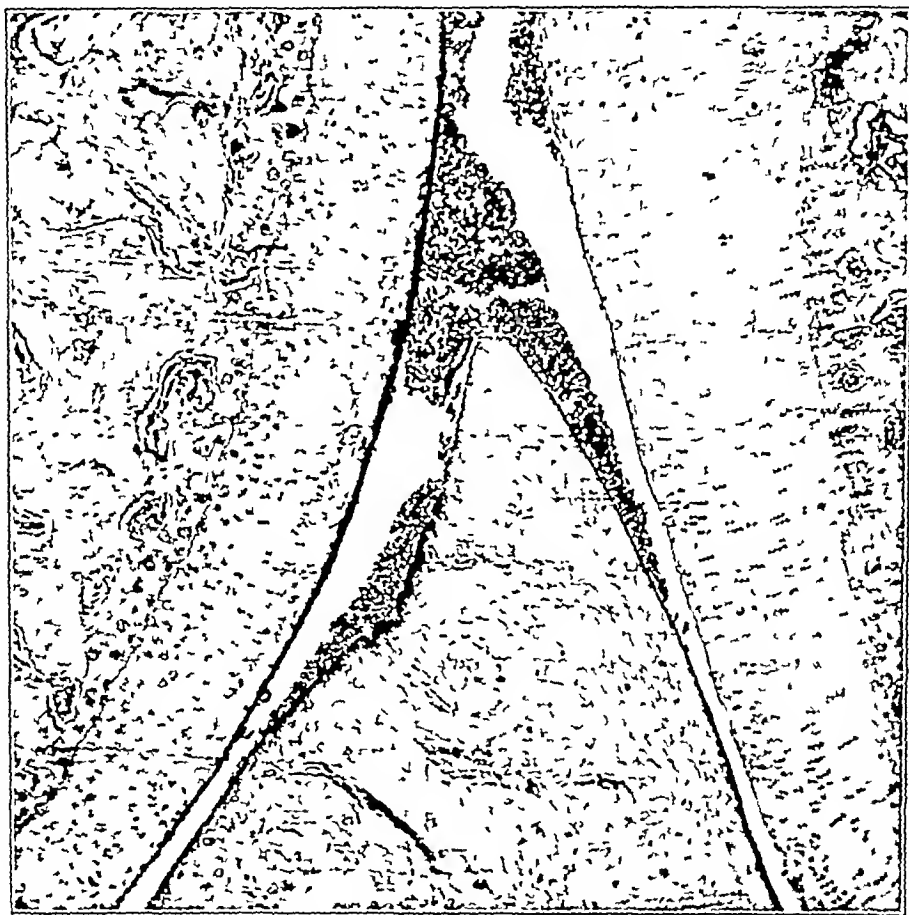


Fig 6—Low power photomicrograph of section from rabbit 4. Died on fifth day after infection of acute diarrhea and prostration. Joint culture positive. Joint received one injection of 0.25 per cent aqueous gentian violet on second day after infection. Pus and fibrin in the joint space and a beginning indentation of the cartilage of the tibia (on the right).

Day 4 Right knee showed same amount of motion, with an increase in the amount of swelling

Day 6 Same as last note

Day 9 Right knee showed 75 degrees' limitation of extension, with a fair amount of swelling and increase in local heat. Aspiration showed a negative culture. Roentgenogram showed a marked clouding of the joint

Day 26 Right knee showed 90 degrees' limitation of extension, with a fair amount of swelling. Aspiration showed a negative culture



*[The page contains dense, handwritten text in Hebrew script, which is heavily tilted and difficult to decipher due to the angle and quality of the scan.]*

Day 51 Right knee showed same amount of motion and swelling Roentgenogram showed a marked irregularity with a destruction of the joint surfaces and clouding of the joint.

Day 82 Right knee showed the same amount of motion and swelling Culture from joint negative

Day 86 Right knee showed 90 degrees' limitation of extension, with a slightly less amount of swelling and no local heat

Autopsy Culture from right knee, negative Roentgenogram of right knee showed a marked destruction of all bony surfaces with a thickening of the head of the tibia and a thinning of the lower end of the femur, with a fusiform shadow along the upper crest of the tibia

The right knee now showed only 45 degrees of limitation of full extension, with a bony hard swelling along the upper tibia and around the condyles of the femur On dissection around the joint a small fusiform purplish tinted caseous mass was found along the upper end of the tibia, which gave the roentgen-ray shadow at this point. On section this was found to be a little gritty When the joint was opened transversely a tremendous amount of fibrous tissue was found in the joint, with a roughening of the upper end of the tibia, and the condyles of the femur The semilunar cartilages and the crucial ligaments could not be clearly ascertained because of the amount of fibrous tissue

Microscopic examination of an extremely poor section from the right knee revealed the following An infiltration of leukocytes could be seen through the joint cavity and muscles, with an engorgement of the vessels The joint lines could not be determined No abscesses were seen The inflammation was apparently slight

RABBIT 6—Sex, male, weight, 2 pounds, 12 ounces (1.2 Kg), age, 3½ months Injection of right knee, Jan 6, 1926, with 0.1 cc of twenty-four hour broth culture of *Staphylococcus aureus*

Day 1 Right knee showed only a small reaction, with about 10 degrees of limitation of extension and a slight swelling

Day 4 Same as on first day

Day 9 The right knee seemed slightly more swollen, with a limitation of the last 20 degrees of extension Aspiration showed a negative culture Injection of 1 cc of 0.25 per cent aqueous gentian violet Roentgenogram showed a slight clouding about the joint.

Day 24 Right knee a limitation of the last 35 degrees of extension, with a small amount of swelling Aspiration showed a negative culture

Day 51 Right knee showed 35 degrees' limitation of extension and same amount of swelling Roentgenogram showed a slight clouding of the joint with an irregularity of the under surface of the patella

Day 82 Right knee showed limitation of last 5 degrees of extension, with slight swelling

Day 86 Right knee showed same amount of motion with a hard swelling around the condyles of the femur

Autopsy Roentgenogram showed a slight irregularity of the upper surface of the tibia, lower surface of the femur and under surface of the patella

There was a slight limitation of full extension of 15 degrees, with no perceptible swelling about the joint Gentian was not found in the tissues The joint was not opened

Microscopic examination of a section from the right knee revealed unusually clear joint lines There was a slight erosion of cartilage on the opposing surfaces, with a small amount of pus and fibrin in the joint Gentian was not seen

in the joint. The cartilages and ligaments were normal throughout. Changes could not be made out.

Microscopic examination of a section of the right knee disclosed little reaction. There were a few breaks in the cartilage of the femur and tibia which were probably artefacts. A slight amount of fibrin was found in the joint, and a small amount of gentian. There was a serosoid bone in the popliteal space.

RABBIT 20—Sex, male, weight, 3 pounds, 12 ounces (17 Kg.), age, 4 months. Injection of right knee with 0.1 cc of a twenty-four-hour broth culture of *Staphylococcus aureus* on March 11, 1926.

Day 18. Right knee showed a large amount of swelling, with increase in local heat and 100 degrees' limit to full extension. Culture from joint positive. Day 23. Knee showed large amount of swelling, especially in the outer lower quadrant of the knee, with increase in local heat and fibrous reaction about the joint. Motion limited 110 degrees. Roentgenogram showed a marked irregularity and destruction of the joint surfaces, with clouding of the joint.

Day 88. The right knee showed a more marked nodular formation about the joint, with the same amount of swelling and limitation of motion. Under iodine technic one or two of the nodules were opened and the pus was evacuated. Day 115. Same method of evacuation of the caseous pus from three more nodules.

Day 128. The right knee showed the same nodular swelling with soft midpoints to the nodules. Motion was not beyond 110 degrees' extension. Day 216. There was the same nodular swelling, with pus draining from one or two points. Joint was ankylosed at an angle of 120 degrees.

Day 230. The same nodular swelling was seen, with draining sinuses at two points, and a limit of 135 degrees to extension. Swelling extended into the popliteal space.

Autopsy. A large number of caseous nodules with thick purulent material about the joint extended down the lower part of the leg and into the popliteal space. The joint was large and thickened. There was a large amount of fibrous tissue and new bone formation in the joint. All the joint structures were obliterated with a complete destruction of all the cartilage. There was the barest semblance of crucial ligaments. No fibrin pus was found in the joint. The patella was large, thick and roughened. Some new bone formation was present in the popliteal space. The motion in the joint was from 160 to 135 degrees.

Microscopic examination of a section of the right knee showed a large number of joint changes. There were two abscesses in the head of the tibia about where the epiphyseal line should be seen. A great deal of pus and fibrous tissue was present through the joint. Cartilage was not present on the lower end of the femur or upper end of the tibia. Small fragments of bone were found in the joint. There were a few islands of cartilage separated from, but adjacent to, the tibia. The bone was eroded in spots at the lower end of the femur. Abscesses were seen in the popliteal space. The inflammatory process looked like one which was healing. The bone marrow in places had been supplanted by fibrous tissue.

RABBIT 21—Sex, female, weight, 4 pounds, 3 ounces (19 Kg.), age, 6 months. Injection of right knee, April 9, 1926, with 0.1 cc of a twenty-four-hour broth culture of *Staphylococcus aureus*.

in the joint or tissues. There was a slight engorgement of the vessels. The patella apparently was normal. A slight amount of fibrous tissue supplanted the bone marrow in the femur. There was a cartilage proliferation from the popliteal side of the tibia. The inflammatory process was like one which has healed.

RABBIT 7—Sex, male, weight, 2 pounds, 14 ounces (1.3 Kg), age, 3½ months. Injection of right knee, Jan. 11, 1926, with 0.1 cc. of a twenty-four hour broth culture of *Staphylococcus aureus*.

Day 1. Right knee showed no limitation of motion, with a slight amount of swelling with no increase in local heat.

Day 4. Right knee showed a limitation of 45 degrees of extension, with a fair amount of swelling and increase in local heat. Culture from joint positive. Injection of 1 cc. of 0.25 per cent aqueous gentian violet. Roentgenogram showed a slight clouding of the joint.

Day 9. Right knee showed the same amount of motion and swelling. Culture from joint positive.

Day 10. Right knee showed the same. Injection of 1 cc. of 0.25 per cent aqueous gentian.

Day 19. Right knee showed a much more marked reaction, with 110 degrees' limitation of extension and much more swelling, with an increase in local heat. Culture from joint was negative.

Day 38. Right knee showed limitation of extension of 135 degrees, with a moderate amount of swelling. Culture from joint negative.

Day 46. Right knee showed about the same amount of motion and swelling. Roentgenogram showed a marked irregularity of all joint surfaces, with a thinning of the lower end of the femur and a clouding about the joint.

Day 52 (autopsy). Culture from right knee was negative.

The skin over the right knee showed a subcutaneous fibrous reaction. There was a limitation of 90 degrees of full extension. Caseous nodules were present about the upper end of the tibia, in the popliteal space and down the outside of the tibia. This latter was fusiform, and purplish tinted. The popliteal swelling seemed to communicate with the joint proper. When the joint was opened, the most noticeable observation was the amount of fibrous reaction and imperceptibility of the joint structures. There was an erosion of the cartilage and bone in the joint.

Microscopic examination of only a fair section from the right knee revealed the following. There was a marked irregularity of the joint surfaces with erosion of cartilage. Little cartilage remained. A large amount of fibrous tissue was seen through the joint, with pus and fibrin. One large abscess was found in the medullary cavity of the tibia and two small ones in the diaphysis close to the epiphyseal line. Gentian was not seen. One of the abscesses in the tibia apparently connected with the joint. The bone marrow in places had been supplanted by fibrous tissue. The inflammatory process was certainly still in the acute stage.

RABBIT 8—Sex, female, weight, 2 pounds, 13 ounces (1.3 Kg), age, 3½ months. Injection of right knee, Jan. 11, 1926, with 0.1 cc. of a twenty-four hour broth culture of *Staphylococcus aureus*.

Day 1. Right knee showed 10 degrees' limitation of full extension, with a slight amount of swelling, and increase in local heat. Injection of 1 cc. 0.25 per cent aqueous gentian violet.

Day 4. Right knee showed 20 degrees' limitation of extension, with a fair amount of swelling and increase in local heat. Culture from joint was positive. Roentgenogram showed a slight clouding of the joint structures.

Day 1 Right knee showed a definite increase in local heat, with a slight swelling but no limitation of motion. Culture from right knee positive. Injection of 1 cc of 0.25 per cent devtrosc gentian violet

Day 3 Right knee showed a slight amount of swelling, with 70 degrees' limitation of full extension and marked increase in local heat. Culture from joint positive. Injection of 1 cc of 0.25 per cent devtrosc gentian

Day 7 Right knee showed a much more marked swelling which had extended down the whole lower part of the leg to the ankle, with 90 degrees' limitation of extension. There was also some limitation of motion in the ankle. Culture from joint negative. Roentgenogram showed a definite clouding of the joint without destruction.

Day 10 Right knee showed a large amount of swelling, with 100 degrees' limitation of extension. There was a nodular swelling on the outer side of the joint. Culture from joint negative.

Day 19 Right knee showed less swelling, with an increase in the motion so that the extension was only limited 60 degrees. Roentgenogram showed a slight clouding and fuzziness of the joint lines.

Day 31 Right knee was almost completely normal, with only small amount of swelling and only a limitation of 10 degrees of full extension. Roentgenogram of right knee was entirely negative.

Day 123 Right knee showed only the slightest limitation of full extension, not over 5 degrees, with absolutely no swelling.

Day 211 The right knee showed normal motion, with no swelling or limit to extension.

Day 225 The right knee showed no swelling, no limit to extension and was, apparently, a perfectly normal joint. Weight, 4 pounds, 9 ounces (2.1 Kg.) Autopsy There was a limit of the last 10 degrees of extension, with a slight fibrous reaction around the joint. Swelling, lateral mobility and pus nodules were not present. There was an erosion of the cartilage on the upper portion of the condyles, with island formation of bits of cartilage. The crucials were present and looked normal. The semilunars looked a little thinner than normal. There was a slight erosion of the cartilage around the top of the tibia on the edges.

Microscopic examination of a section from the right knee showed remarkably little reaction in the joint. A small amount of fibrous tissue was found in the joint. No pus in the joint but some in the surrounding tissues. The crucials were present. The cartilage was denuded in spots over both surfaces of femur and tibia. No abscess formation. Large amount of fibrous tissue in popliteal space. The cartilage had proliferated in spots. The bone marrow was sup- planted in places with fibrous tissue but this was not marked. The inflam- matory process was distinctly one which had healed.

Rabbit 22—Sex, female, weight, 2 pounds, 10 ounces (1.25 Kg.), age, 3 months. Injection of the right knee, April 16, 1926, with 0.1 cc of a twenty- four-hour broth culture of *Staphylococcus aureus*.

Day 1 Right knee showed a slight increase of local heat and swelling, with 10 degrees' limitation of extension. Culture from joint positive. Injec- tion of 1 cc of 0.5 per cent olive oil gentian violet.

Day 3 Right knee showed about 60 degrees' limitation of extension, with slight amount of swelling and local heat increase. Culture from joint positive. Injection of 1 cc of 0.5 per cent olive oil gentian

Day 4 Right knee showed same amount of motion and slightly more swelling. Culture from joint positive. Injection of 1 cc of 0.5 per cent olive oil gentian

Day 9 Right knee showed same condition Injection of 1 cc of 0.25 per cent aqueous gentian

Day 11 Right knee showed more marked reaction, with only 90 degrees' extension and slightly more swollen, with swelling in nodules above the patella Culture from joint positive

Day 19 Right knee showed limitation of 120 degrees' extension, with about the same swelling and local heat Culture from joint positive

Day 21 Knee showed same condition Injection of 1 cc 0.25 per cent aqueous gentian

Day 22 Right knee showed a slight increase in swelling with same motion and increase in local heat Culture from joint negative

Day 38 Knee showed same amount of swelling and motion Culture from joint negative

Day 46 Knee now showed a limitation of 75 degrees of motion, with same swelling Roentgenogram showed a marked destruction of the joint surfaces, especially the condyles of the femur and the under surface of the patella, with a few shadows around the joint suggesting gentian infiltration in the tissues

Day 52 (autopsy) Culture from joint negative

There was a fibrous reaction in the subcutaneous tissue around the right knee with a slight adherence of the skin There were many purplish tinged caseous nodules in the fascia, and extending down into the popliteal space The joint was opened transversely A large amount of fibrous tissue in the joints bound other elements down tightly The cartilages were eroded and the bony surfaces were roughened Gentian was not found in the joint, and there was no evidence of frank pus in the joint There was a contracture of the hamstrings

Microscopic examination of a poor section from the right knee disclosed the following There was a fair amount of fibrous tissue reaction with infiltration of pus about the joint An infiltration of pus and gentian was observed in the muscles, with an engorgement of vessels

RABBIT 9—Sex, female, weight, 3 pounds, 5 ounces (1.5 Kg), age, 3½ months Injection of right knee, Jan 16, 1926, with 0.1 cc of a twenty-four hour broth culture of *Staphylococcus aureus*

Day 1 Right knee showed a slight amount of swelling, with limitation of 15 degrees' extension and increase in local heat Culture from joint positive Injection of 1 cc of 0.25 per cent aqueous gentian violet

Day 2 Right knee showed slight increase in swelling, with 20 degrees' limitation of extension and increase in local heat Culture from joint positive Roentgenogram showed a slight clouding of the joint

Day 3 Right knee showed 90 degrees' limitation of extension, with slight increase in swelling

Day 4 Right knee showed same size and amount of motion Injection of 1 cc 0.25 per cent aqueous gentian

Day 6 Right knee showed 100 degrees' limitation of extension, with swelling well up into the suprapatellar pouches Culture from joint positive

Day 14 Right knee had a limitation of 120 degrees' extension, with swelling more marked, there being nodules to the medial side of the joint Culture from joint positive

Day 33 Right knee showed 100 degrees' limitation of extension, with moderate amount of swelling Reaction was less than last note Culture from joint showed only one colony of *Staphylococcus aureus*

Day 6 Right knee showed 80 degrees' limitation of extension, with same amount of swelling and local heat increase Culture from joint positive

Day 7 Knee showed 100 degrees' limitation of extension, with same amount of swelling Roentgenogram showed a slight clouding of the joint

Day 18 Knee showed 135 degrees' limitation of extension, with large amount of swelling, especially in the upper pouches of the joint Culture from joint negative

Day 24 Joint showed marked swelling extending down the lower part of the leg, with nodule formation, and limitation of 120 degrees' extension Culture showed a small growth Roentgenogram showed a marked irregularity of the joint line, with destruction of the joint surfaces and a thinning of the lower end of the femur

Day 31 (autopsy) Culture showed a negative growth Roentgenogram showed the same joint changes as were seen in the last roentgenogram, with less clouding about the joint

When the skin was removed there was a limitation of about 120 degrees of full extension, with nodule formation down the inner side of the lower part of the leg Some gentian was found in the popliteal space There was a roughening on the under surface of the patella and on the lower surface of the femur A small amount of pus was present on the joint The cartilages were pretty well destroyed All the crucial ligaments were thinned but not destroyed There was a great deal of fibrous tissue in the posterior portion of the joint which seemed to limit full extension, with a thickening of the capsule

Microscopic examination of a section from the right knee did not show the tibia clearly, but the changes in the femur were plain There was an erosion of all the cartilage, with the exception of a few islands The cartilage had been replaced by fibrous tissue There was a large abscess containing islands of cartilage which extended through the epiphyseal line of the femur well encapsulated There was a good deal of fibrous tissue through the joint Pus was found through the muscles The inflammatory process looked like one which was becoming progressively more acute The fibrous tissue in places had supplanted the bone marrow

RABBIT 23—Sex, male, weight, 3 pounds (1.4 Kg), age, 3 1/2 months Injection of right knee, April 16, 1926, with 0.1 cc of a twenty-four-hour broth culture of *Staphylococcus aureus*

Day 1 Right knee showed a fair amount of swelling, with increase in local heat and limitation of last 15 degrees of extension Culture from joint negative Injection of 1 cc of 0.25 per cent dextrose gentian violet

Day 3 Right knee showed moderate amount of swelling, with limitation of 75 degrees of extension Culture from joint positive Injection of 1 cc of dextrose gentian violet

Day 4 Right knee showed more marked swelling, with 110 degrees' limitation of extension and increase in local heat Culture from joint negative Injection of 1 cc of 0.25 per cent dextrose gentian

Day 6 Swelling of right knee was even more marked, with 120 degrees' limitation of motion and increase in local heat Culture from joint negative

Day 7 Right knee showed same swelling and motion Roentgenogram showed a clouding of the joint with a slight fuzziness of the posterior portion of the tibia

Day 24 Right knee showed 135 degrees' limitation of extension with a large amount of swelling which was of the nodular type Roentgenogram showed a marked clouding of the joint with a destruction of the joint line and a thinning of the lower femur

Day 41 Right knee showed same swelling and motion. Roentgenogram showed a marked destruction of the joint with a thinning of the condyles of the femur and a thickening of the upper end of the tibia, and a clouding of the whole joint.

Day 53 (autopsy) Culture from right knee negative.

Gentian or pus was not discovered in the surrounding tissues. When the joint was opened the large amount of fibrous reaction in the joint was most marked. All the cartilages were destroyed with a roughening of all bony surfaces. The fibrous tissue had completely filled the joint. Pus or gentian were not found in the joint.

Microscopic examination could not be performed because the specimens were lost.

RABBIT 10—Sex, male, weight, 3 pounds, 8 ounces (1.6 Kg), age, 4 months. Injection of right knee with 0.1 cc of a twenty-four hour broth culture of *Staphylococcus aureus* on Jan 16, 1926.

Day 1 The right knee showed a slight amount of swelling, with increase in local heat, tenderness and limitation of the last 15 degrees of extension. The rabbit looked toxic.

Day 2 Right knee was more swollen, with more local heat increase and limit to last 30 degrees' extension. Roentgenogram showed a slight clouding about the knee joint. Culture from joint showed moderate growth. Injection of 1 cc of 0.25 per cent aqueous gentian.

Day 3 Knee joint showed a fair amount of swelling, with limit of 90 degrees' extension and more increase of local heat. Rabbit had lost weight. Weight, 3 pounds, 2 ounces (1.4 Kg). Culture from joint positive. Aspirated cloudy bloody fluid.

Day 4 Knee was same as on third day. Injection of 1 cc 0.25 per cent aqueous gentian.

Day 6 The right knee showed more swelling, this being marked in the suprapatellar pouches, with same amount of motion. Culture positive from joint. Aspirated thick purulent material which was slightly purple.

Day 14 Knee was more swollen, with limit of 110 degrees' full extension with fluctuant swelling up into pouches above the knee. Weight, 2 pounds, 14 ounces (1.2 Kg). Culture from joint showed good growth of organism.

Day 33 There was 120 degrees' limit to motion, with moderate amount of swelling. Culture from joint positive.

Day 41 Right knee showed same swelling and motion with more crepitation about the joint. Roentgenogram showed a marked destruction about the joint with a thinning of the condyles of the femur and thickening of the upper end of the tibia, with evidence of destruction on the under surface of the patella. Some shadows were also seen behind the joint.

Day 72 A moderate amount of swelling was present about the joint, with nodule formation and a limit of 120 degrees of extension. Culture showed a good growth of the organism. Aspiration of thick grumous material.

Day 76 The right knee showed the same nodular swelling, especially on the inner side of the joint, with a thickening of the upper tibia.

Autopsy Culture from right knee positive.

There was a marked swelling about the right knee in large nodular masses, which contained creamy yellow material, especially on the inner upper aspect of the lower part of the leg. Extension was not possible beyond 120 degrees. When the joint was opened a thinner caseous material was encountered. There was a large amount of fibrous tissue throughout the joint with a lateral disloca-



Day 31 (autopsy) Culture from right knee negative Roentgenogram showed same irregularity and destruction, with more thinning of the lower end of the femur. There were many nodules about the joint with a swelling of the joint. Gentian was found in the foreleg and about the joint. When the joint was opened a large amount of purplish purulent material was found. The crucial ligaments and semilunar cartilages were thinned but not altogether destroyed. There was only a slight roughening of the cartilage on the under surface of the patella and condyles of the femur. The impression was that not as much reaction had occurred in this joint as in some of the others, with the same amount of swelling and limitation of motion.

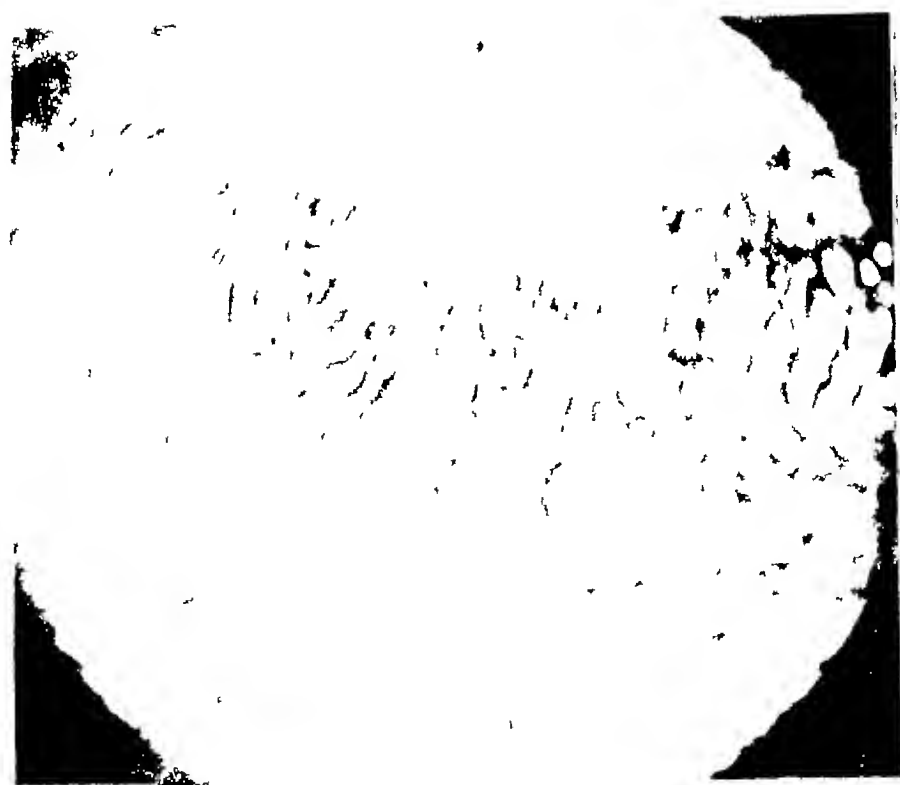
Microscopic examination of a section from the right knee revealed a marked reaction in the joint. All the joint surfaces were irregular, with an erosion of joint cartilage, only a small amount being left intact in the anterior part of the femur which had fibrous tissue growing into it. A large amount of pus and fibrous tissue was present in the joint. The bone was eroded in spots. There was one place where the bone and cartilage have sequestered off. A large abscess was seen in the upper diaphysis of the tibia. There were several abscesses in the popliteal space and pus under the periosteum in the anterior part of the femur. The fibrous tissue was suppurating the bone marrow in places. The inflammatory process was subsiding.

Rabbit 24—Sex, male, weight, 3 pounds, 8 ounces (1.6 Kg), age,  $3\frac{1}{3}$  months. Injection of right knee, April 19, 1926, with 0.1 cc of a twenty-four-hour broth culture of *Staphylococcus aureus*.

Day 1 Right knee showed a slight amount of swelling, with limitation of last 15 degrees of extension and increase in local heat. Culture from joint positive. Injection of 1 cc of 0.5 per cent olive oil gentian violet. Day 2 Right knee showed same amount of swelling, with 20 degrees' limitation of extension and increase in local heat. Culture from joint positive. Injection of 1 cc of 0.5 per cent olive oil gentian. Day 3 Right knee showed a much more marked reaction, with more swelling extending down lower part of leg into ankle and foot with much more local heat and a limitation of 90 degrees of full extension. Culture from joint showed a small growth. Injection of 1 cc of 0.5 per cent gentian in olive oil. Day 4 Right knee about the same, with perhaps 100 degrees' limitation of motion. Roentgenogram showed a clouding of the joint.

Day 9 Right knee showed less swelling which now extended only to ankle and not into foot, with 90 degrees' limitation of extension. Culture from joint showed small growth. Day 15 Right knee showed perhaps less swelling down the lower part of the leg, but the same about the knee, with limitation of 75 degrees' extension. Culture from joint did not show growth. Day 21 Right knee showed the same swelling, with 70 degrees' limitation to extension. Culture showed a small growth after forty-eight hours. Roentgenogram showed a slight haziness about the joint, with some irregularity and thickening of the lower femur.

Day 28 (autopsy) Culture from joint negative. Roentgenogram showed same picture as last described, with slightly less irregularity. Before the skin was removed there was about 75 degrees' limitation of motion, with some grating and lateral mobility in the joint. Pus was present in gentian tinted nodules down the lower part of the leg. There was thin mucoid pus in the joint, with small bodies suggesting rice bodies. The liga-



18 and 21) Further, it was pointed out that in the fifty cases undergoing spontaneous remission these areas of hyperinvolution became reinvolved in subsequent exacerbations of the morbid process, hypertrophy and hyperplasia. This was to be expected in view of the fact that they were a portion of the parenchyma. Since the clinical tumors in this group of thirty-seven cases presented the microscopic appearance identical with that of the involutinal bodies or areas of hyperinvolution, since they had become involved with the remainder of the parenchyma in the present exacerbation, and since numerous remissions and exacerbations had occurred in the clinical course of the disease process

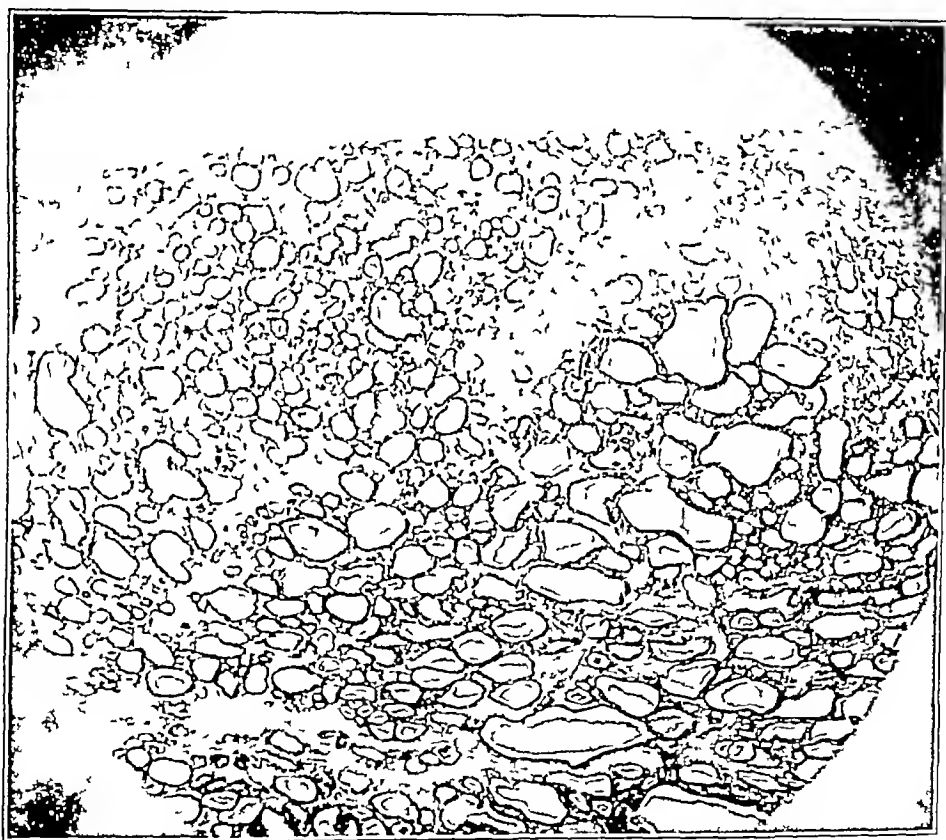


Fig 24 —Higher power magnification of figure 23 showing in detail the typical disintegration toward the center of the localized area of hypertrophy and hyperplasia. This results, as is plainly seen, in a diminution of the actual number and size of the functioning parenchyma with a resultant substitution by fibrous connective tissue. These changes as shown are regressive involutinal changes of a degenerative nature, the opposite of the aggressive or regenerative changes characteristic of a true benign neoplasm. Reduced from a magnification of  $\times 57$ .

in these cases, it would seem highly probable that the tumors or nodules in these cases were the result of the long continued hyperthyroidism, and that they did not play a part in the production of the present clinical signs and symptoms anymore than did any other portion of the parenchyma.

ments looked fairly normal with some roughening of the cartilage. The semilunars looked normal. A peculiar bony nodular swelling was observed on the condyles of the femur.

Microscopic examination of a section from the right knee showed a fair amount of reaction. There was an irregularity of the cartilage mainly of the opposing surfaces. A fair amount of fibrous tissue was found in the joint, with pus and fibrin. The largest part of the cartilage was replaced by fibrous tissue. Fragments of bone and cartilage were present in the joint. There was fibrous tissue in the joint attached to cartilage. The anterior part of the femur was well preserved with cartilage. A sesamoid bone was present in the popliteal space. There was no abscess formation. In places the bone marrow had been supplanted by fibrous tissue. The inflammatory process was in the subacute stage.

RABBIT 25—Sex, male, weight, 3 pounds, 2 ounces (1.45 Kg.), age, 3½ months. Injection of right knee with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus* on April 19, 1926.

Day 1. There was a slight amount of swelling in the joint, with increase in local heat and restriction of 25 degrees' extension. Culture from joint positive. Injection of 1 cc. of 0.5 per cent olive oil gentian violet.

Day 2. Right knee showed the same reaction. Culture from joint positive. Injection of 1 cc. of 0.5 per cent olive oil gentian.

Day 3. Right knee showed a limitation of 75 degrees' extension, with same amount of swelling and increase in local heat. Gentian recovered in aspiration. Culture from joint showed a small growth. Injection of 1 cc. of 0.5 per cent olive oil gentian.

Day 4. There was a more marked reaction with 110 degrees' limitation of extension and the same amount of swelling. Roentgenogram showed a clouding of the joint.

Day 9. There was an increase of the motion to 45 degrees' limitation of extension, with probably more marked swelling and less local heat. No gentian now in the aspiration. Culture from joint showed small colonies of the *Staphylococcus aureus*.

Day 15. The same amount of swelling was filling the outer pouches of the knee, and extension was limited 60 degrees. Culture from joint showed few small colonies.

Day 21. There was less swelling with same motion as last noted. Culture showed one small colony in forty-eight hours.

Day 28 (autopsy). Culture from knee negative. Roentgenogram showed a marked haziness about the joint, with an irregularity of the upper tibia and the lower femur.

There was a large amount of purplish tinged pus in the tissues of the lower part of the leg. The joint capsule was distended with a light mucoid material. There was a limitation of the full extension of 60 degrees. There was a definite grating of the patella on the femur. A moderate amount of swelling was present about the joint. The joint was not opened.

Microscopic examination of a section from the right knee disclosed erosion of the cartilage in several places. The cartilage on the tibia had fibrous tissue growing beneath, and in places along the femur cartilage was growing out into the fibrous tissue. A small amount of pus and fibrin was present in the joint with a fair amount of fibrous tissue. There were thickened synovial tags. The semilunar cartilages were intact. There was a replacing of the bone marrow with fibrous tissue. The inflammatory reaction was still in the acute stage.

# THE TRANSFUSING OF UNMODIFIED BLOOD

IV EXPERIENCE IN NEARLY TWO THOUSAND, FIVE HUNDRED CASES CHANGES IN APPARATUS \*

OSBORNE ALLEN BRINES, M.D

Pathologist to Receiving, the Jefferson Clinic and Eloise Hospitals

DETROIT

The progress and results of blood transfusion at this clinic, first with the Unger<sup>1</sup> apparatus and then with my modification<sup>2</sup> of the Unger apparatus, have previously been discussed in part by Dr Blain and me<sup>3</sup> With these two types of apparatus, which were somewhat similar, nearly 2,500 transfusions of unmodified blood have been performed The method has proved satisfactory and leaves little to be desired The method provides for a continuous flow of blood from the donor to the recipient with scarcely any clotting, because stagnation is eliminated The maximum of speed is acquired, the time necessary for the actual transfusion of 500 cc being about five minutes Many of the transfusions have required even less time, and it has never been observed that the blood was given too rapidly Foreign material is not introduced during the transfusion, with the exception of 3 or 4 cc of saline before any blood passes through the apparatus, and this is for the purpose of demonstrating the correct position of the needle in the recipient's vein

There have not been any deaths directly attributable to transfusion in the series Transfusion may have been a contributing factor in the cause of death in three cases of nephritis My experience, naturally, added to the observations of others, leads me to suspect that nephritis might constitute a contraindication to transfusion The only other contraindications are pulmonary edema and a damaged myocardium Although I have never observed unfavorable consequences following transfusion in cases of heart lesions, I would advise caution

The criteria of a post-transfusion reaction should include, in addition to a mere elevation of temperature, some definite subjective or objective symptoms, such as a chill, pain, dyspnea, urticaria, hemoglobinuria and jaundice

\*From the Jefferson Clinic and Diagnostic Hospital

- 1 Brines, Osborne A The Transfusing of Unmodified Blood Arch Surg 7 306 (Sept) 1923
- 2 Brines, Osborne A The Transfusing of Unmodified Blood II The Technique in 1000 Cases, Arch Surg 12 124 (Jan) 1926
- 3 Blain, Alexander W, and Brines, Osborne A The Transfusing of Unmodified Blood III The Clinical Aspect of 1000 Cases, Arch Surg 12 140 (Jan) 1926

RABBIT 26—Sex, male, weight, 3 pounds, 4 ounces (1.5 Kg), age, 3½ months  
Injection of right knee with 0.1 cc of a twenty-four-hour broth culture of *Staphylococcus aureus* on April 20, 1926

Day 1 Right knee showed a slight swelling, with limitation of last 10 degrees of motion and increase in local heat. Culture from joint positive.  
Injection of 1 cc of 0.5 per cent olive oil gentian violet

Day 2 A marked swelling of the knee extended down the ankle to the foot, with a limitation of 90 degrees of full extension, and an increase in local heat. Culture from joint positive. Injection of 1 cc of 0.5 per cent olive oil gentian violet

Day 3 Knee showed limitation of 110 degrees' full extension with same swelling down leg to ankle and foot. Culture from joint positive. Injection of 1 cc of 0.5 per cent olive oil gentian. Roentgenogram showed a slight clouding of the joint

Day 8 There was more marked swelling of the whole knee, lower part of the leg and foot with motion limited 100 degrees. Culture from joint positive

Day 14 There was a more nodular swelling around the knee which extended down the foreleg to the ankle. At the ankle there was an open draining sinus from which gentian tinted pus could be expressed. A culture from this showed the same organisms. The motion at the knee and ankle was limited 90 degrees. Culture from knee joint showed positive growth

Day 20 Right knee showed the same nodular swelling, with a limitation of extension of 100 degrees. The swelling down the leg was not as marked. The motion in the ankle was now limited only 30 degrees. There was a scab over the sinus at the ankle. Culture from knee showed one colony after forty-eight hours. Roentgenogram showed a haziness about the joint surface, with an irregularity of the upper tibia and lower femur, with a thickened nodule on the femur

Day 27 (autopsy) Culture from knee was negative. Roentgenogram showed same condition as on twentieth day

A rather large nodular swelling was seen about the joint and a distention of the joint capsule proper. A good deal of caseous looking gentian tinted pus was present in the popliteal space and around the joint, also down the lower part of the leg. There was a definite increase in the mobility of the joint with a grating on motion. The joint was not opened

Microscopic examination of a section from the right knee revealed a large amount of reaction and destruction in the joint. There was a marked irregularity of the joint surfaces. All the cartilage was eroded except that on the anterior surface of the femur. Fissures were present in the cartilage on the tibia. A large amount of fibrous tissue and pus was found in the joint. There were abscesses anterior to the head of the tibia and in the popliteal space. Thickened synovial membrane in the popliteal area. There was a small sesamoid bone anterior to the femur, which might have been the patella but was not altogether typical of this. Thickened crucial ligaments were present. In places, the bone marrow had been supplanted by fibrous tissue. The inflammatory process was fairly acute

RABBIT 27—Sex, female, weight, 3 pounds, 8 ounces (1.6 Kg), age, 3½ months. Injection of right knee with 0.1 cc of a twenty-four-hour broth culture of *Staphylococcus aureus* on June 3, 1926

Day 1 Right knee showed a fair amount of swelling and increase in local heat, with limitation of 10 degrees' extension. There was also a swelling of the glands in the right groin. Culture from joint positive. Injection of 1 cc of 0.5 per cent dextrose gentian violet

In nearly 2,500 cases in which transfusion was used, only three patients had severe post-transfusion reactions. All were purely anaphylactic in type and occurred with sudden onset immediately following the transfusion. One reaction was extremely severe and the other two moderately severe.

One of the less severe reactions consisted of a convulsion followed by coma and accompanied by an increase in pulse rate and a decrease in the volume of the radial pulse, shallow and slowed respirations and cyanosis, all of which lasted about thirty minutes and were immediately followed by complete recovery.

The most severe reaction consisted of a convulsion and then coma, cyanosis and shallow respiration, the respiratory rate dropping to 2 or 3 a minute, and complete disappearance of the radial pulse and inaudible heart sounds. This state lasted about half an hour, after which the pulse and respiration became satisfactory, the patient reacted to his surroundings at the end of an hour, but remained more or less delirious for several hours.

The third reaction occurred in one of the cases of nephritis mentioned, and the initial symptom was a sudden onset of severe generalized abdominal pain which, after about ten minutes, shifted to the lumbar region. The pain was relieved by the administration of morphine sulfate,  $\frac{1}{2}$  grain (0.03 Gm.), but a severe chill accompanied by an elevation in temperature of  $4^{\circ}\text{F}$  followed. The reaction in this form was intermittent and lasted with diminishing severity for about thirty-six hours. Uremic symptoms became conspicuous and death occurred in five days. A careful recheck of grouping and crossagglutination failed to reveal the slightest incompatibility in any of these three cases.

Crossagglutination as a routine procedure was abandoned as unnecessary and superfluous in the laboratory of the Jefferson Clinic four years ago, when we began to use group IV (Moss) agglutinating serum in addition to the usual group II and group III serums. By this means, we are able to detect deterioration of either group II or group III serum. Errors in blood grouping are usually not due to poor laboratory technique but to a sudden reduction in titer of the known serums. It is a well known fact that agglutinating serum may possess sufficient titer today but tomorrow may be absolutely useless. In some laboratories where several days and even weeks may elapse between requests for blood grouping, the serums employed are not reliable without this additional safeguard, which depends on the fact that if there is agglutination with group IV serum, there must be agglutination with either group II or group III serum or both. When agglutination is produced with group IV serum alone, one of the other serums must be impotent, and an investigation can be made. The most common error in grouping, and the only one that I have personally witnessed, is placing a group II

Day 2 There was more swelling, with an increase in local heat and limitation of last 45 degrees of extension Gentian was aspirated from the joint Culture from joint negative Injection of 1 cc of 0.5 per cent dextrose gentian

Day 3 Joint showed a slight decrease in the swelling and local heat, and 30 degrees' limitation of motion Crepitation was present in the suprapatellar pouches Gentian aspirated Culture from joint negative

Day 4 Knee showed same amount of swelling, with crepitation and 45 degrees' limit to full motion Culture from joint negative

Day 9 Joint showed same amount of swelling, with no increase in local heat and 100 degrees' limitation of full extension Culture from joint negative Roentgenogram showed a slight haziness about the joint

Day 13 Knee showed slightly less swelling and 90 degrees' limitation of extension Small amount of caseous gentian tinted tissue aspirated Culture from joint negative

Day 18 Joint showed a moderate amount of swelling, with an increase in the size of band running from the joint up to the groin There was 90 degrees' limit to full extension Gentian aspirated Culture from joint negative

Day 68 The knee showed about the same swelling and a limit of extension of 90 degrees There was some crepitation of the tissues and a nodule in the upper inner pouch about the joint

Day 156 The right knee could not be extended beyond 90 degrees There was no swelling The rabbit looked sick and emaciated There was an extensive ulceration over the right buttock extending up to the flank

Day 160 The rabbit died of malnutrition and weakness Autopsy was not performed

RABBIT 28—Sex, male, weight, 3 pounds, 13 ounces (1.7 Kg), age, 4 months Injection of right knee with 0.1 cc of a twenty-four-hour broth culture of *Staphylococcus aureus* on June 3, 1926

Day 1 Right knee showed a slight amount of swelling, with increase in local heat and 5 degrees' limitation of extension Culture from joint positive Injection of 1 cc of 0.5 per cent dextrose gentian

Day 2 Right knee showed a marked amount of swelling which had extended down the whole lower part of the leg into the foot, with 75 degrees' limitation of extension Culture from joint positive Injection of 1 cc of 0.5 per cent dextrose gentian

Day 3 Joint showed about the same amount of swelling extending down the leg to the foot, with slightly less limitation of extension to 60 degrees and an increase in local heat Culture from joint positive Injection of 1 cc of 0.5 per cent dextrose gentian

Day 4 Joint showed the same amount of swelling with 80 degrees' limitation of extension Gentian aspirated from joint Culture from joint negative

Day 9 Joint showed essentially the same swelling with 90 degrees' limit to full extension Gentian aspirated Culture from joint negative Roentgenogram of joint did not show any changes

Day 13 Knee showed about the same swelling and motion Thin gentian aspirated Culture negative

Day 18 The right knee seemed much improved, with less swelling and 75 degrees' limit to extension Thin gentian aspirated Culture from joint negative

Day 50 The rabbit died of unknown cause Autopsy was not performed

RABBIT 29—Sex, male, weight, 3 pounds, 5 ounces (1.55 Kg), age 3½ months Injection of right knee with 0.1 cc of a twenty-four-hour broth culture of *Staphylococcus aureus* on June 3, 1926



(Moss) individual in group IV, and probably the most important reason for this error is the use of old group III serum due to the difficulty or inconvenience experienced in securing group III serum because of the small number of group III individuals. The use of group IV serum is not an infallible check, but will practically eliminate all error, because it is unlikely that two of the agglutinating serums will deteriorate at the same time, besides, on account of the prevalence of group IV individuals, fresh group IV serum can be obtained frequently—every two or three days—and therefore can be regarded with the greatest confidence. The only error that cannot be guarded against by the use of group IV serum is that of mistaking a group I for a group II or a group III individual, the reason for this is that the cells of a group I individual are agglutinated by both groups II and III serum, and impotence of one or the other would not be detected by this method. The small number of group I individuals minimizes the importance of this danger, and the possibility of such a mistake argues for the more extensive use of universal donors. Since the introduction of group IV serum in the laboratory as a check on the potency of group II and group III serums, errors in grouping have not been made.

In my experience, incompatible blood was used in six transfusions. Four of these errors in grouping occurred in laboratories other than this one, and two occurred in the laboratory before I began to use group IV serum. No casualties resulted in four cases. In one of the other two, death was inevitable and was perhaps hastened by the transfusion. Suspicion regarding compatibility was aroused by the sudden cyanosis of the patient when about 200 cc of blood had been introduced. The other case was one of the three cases of nephritis mentioned before. The patient was moribund, and when about 100 cc of blood had been introduced, dyspnea was suddenly observed. The transfusion was stopped because of the belief that incompatible blood was being used. A severe reaction consisting of a chill and dyspnea occurred, and death followed in three days. In all six cases, group II blood was given to group IV patients. In one case, the error was a clerical one in reporting. In these two cases just described, one patient was comatose and the other was semiconscious, if the operator is reasonably careful and alert, it is only in this type of case that a fatality may follow the use of incompatible blood. The nervous reaction of these patients is too sluggish to detect or to betray the aura of a transfusion reaction, and before it becomes evident that the patient is not behaving normally, a sufficiently large quantity of blood to produce serious consequences has been given. It is likely that a patient who is fully conscious will inform the operator, who should always have in mind the possibility of using incompatible blood, of the first unusual or uncomfortable sensation, which is commonly lumbar or mediastinal pain or respiratory difficulty. Such warnings

Day 1 Right knee showed a slight amount of swelling, with increase in local heat, and about 5 degrees' limitation of full extension Culture from joint positive Injection of 1 cc of a 0.5 per cent dextrose gentian preparation An extravasation of this took place into the tissues on the inner side of the knee

Day 2 Knee showed a moderate amount of swelling, with 60 degrees' limitation of extension and marked increase in local heat Culture from joint positive Injection of 1 cc of 0.5 per cent dextrose gentian

Day 3 Right knee showed an increase of the same swelling up into the groin with marked crepitation of the tissues and 75 degrees' limitation of full extension Culture from joint showed a small growth Gentian aspirated Injection of 1 cc of 0.5 per cent dextrose gentian

Day 4 Right knee showed the same amount of swelling, which had now extended down into the lower part of the leg, with 90 degrees' limit to full extension Culture from joint negative Gentian aspirated

Day 9 Right knee showed slightly less swelling, with crepitation up into the thigh and 100 degrees' limit to full extension Cultures from joint negative Gentian aspirated Roentgenogram of the right knee did not show any changes in the joint This picture showed the same appearance of the joint as that taken before infection

Day 13 Right knee showed fair amount of swelling, with 110 degrees' limit to full extension, crepitus in the joint and a small ulceration below the knee Weight, 3 pounds, 7 ounces (1.6 Kg) Culture from joint negative Gentian aspirated

Day 18 The right knee showed a marked improvement, with only a small amount of swelling and 60 degrees' limit to full extension Culture negative Gentian aspirated

Day 21 (autopsy) Culture from right knee negative

There was more than 45 degrees' limit to full extension, with a fair amount of swelling A purple tinge was present all about the joint when it was opened An air space was found up in the groin The gentian was found down the outer side of the lower part of the leg, almost to the ankle When the joint was opened transversely, it was found to be filled with gentian Pus was not present in the joint Close examination of the ligaments and cartilage in the joint revealed no change The gentian was also in the popliteal tissues Limitation of motion could not be demonstrated after the joint was opened

Microscopic examination could not be performed because the specimens were lost

RABBIT 30—Sex, female, weight, 3 pounds, 4 ounces (1.5 Kg), age, 3½ months Injection of right knee with 0.1 cc. of a twenty-four-hour broth culture of *Staphylococcus aureus* on June 3, 1926

Day 1 Right knee showed a slight amount of swelling, with increase in local heat and 5 degrees of limitation of extension Culture from joint showed good growth Injection of 1 cc of 0.5 per cent dextrose gentian

Day 2 Knee showed increase in swelling, with increase in amount of local heat and 20 degrees' limit to extension Culture from joint negative Aspiration showed gentian Injection of 1 cc of 0.5 per cent dextrose gentian

Day 3 Joint showed slight increase in local heat, with less swelling and 30 degrees' limit to extension Culture from joint negative Gentian aspirated

Day 4 Joint showed 45 degrees' limit to extension and same amount of swelling, with crepitation up into the groin Culture did not show growth Gentian aspirated

symptoms will usually occur before 40 cc of blood has been given, and if the transfusion is discontinued promptly, nothing more serious than a mild or moderately severe reaction will result.

There is one type of post-transfusion reaction which is seldom mentioned and has received little attention, but which occurs with mild symptoms in a small percentage of cases, that is the delayed reaction. I was slow in appreciating the existence of such a type of reaction, because as a rule I did not observe the occurrence myself, and when I was occasionally told that a patient who had received a transfusion in the morning had a mild or moderately severe chill that night or the next day, lasting sometimes for an hour or more, I was inclined to consider this a mysterious affair unrelated to the transfusion, because I was sure that if a reaction did not occur within two hours, none would occur. The delayed reaction is now recognized but a possible explanation for such a phenomenon cannot be suggested.

As far as I know, embolism has never been produced during a transfusion given by my associates or me. I have never seen a case of air embolism, but I recognize that there is danger of such an occurrence, and I never inject more than a few very small bubbles of air.

In only two cases in this series did the attempt to perform a transfusion fail because of inability to introduce the needle into the patient's vein. The first case was that of an infant, and this incident has been described in a previous article.<sup>2</sup> The second unsuccessful attempt was made in the case of an obese woman who had received two transfusions within the preceding two or three weeks. Both arms had been used, and on each side an incision had been made and the vein exposed but not transected or ligated. The third transfusion for this patient, who was a poor surgical risk, was attempted in the operating room at the end of an abdominal operation. Incisions in the arms were necessary, but a mistake was made in that the new incisions were parallel to the old ones, instead of being started where the previous ones ended. The veins which had been entered before were tried this time, and in each arm the vein parted at the old site of venous puncture when the pressure of the needle was exerted, and the proximal end of the vein could not be picked up and no other veins could be readily found. Before another location could be selected, the patient died. The technic was admittedly faulty, and a different line of attack would be employed in a similar case in the future. The use of universal donors is becoming more popular continually. One feels safer and less apprehensive of undesirable sequelae when the donor is in group IV. The records show that the smallest percentage of post-transfusion reactions has occurred when the donor has been in group IV, regardless of whether the recipient is in group I, II, III or IV, and the largest percentage of reactions has occurred when both donor

Day 9 Right knee showed same swelling, with 75 degrees' limit to extension and little crepitus Culture from joint was negative, gentian aspirated Roentgenogram did not show changes

Day 13 Joint showed same swelling, with less limitation of extension, this being now 40 degrees The rabbit showed a marked loss of weight Weight, 2 pounds, 11 ounces (1.2 Kg) Culture from joint negative Gentian aspirated

Day 18 Right knee was almost normal, with just a little limitation of extension, about 5 degrees, and the slightest amount of swelling Culture negative Gentian aspirated

Day 55 There was no limitation of motion, with no swelling A small scab was seen on front surface of knee beneath which a little pus was found

Day 68 Knee joint showed a small amount of swelling with about 10 degrees' limitation to full extension

Day 156 The right knee showed a distinct lateral dislocation with apparent evidence of the crucial ligaments being relaxed There was about 70 degrees' external rotation with 30 degrees of abduction and 45 degrees' limitation to full extension Swelling was not present

Day 170 The knee showed a limit of 90 degrees to full extension, with the same lateral displacement Weight, 4 pounds, 8 ounces (2 Kg)

Autopsy The joint was opened transversely across the patellar tendon Pus and gentian were not found in the joint There was a marked erosion of all the cartilage over the condyles of the femur, with small islands of cartilage remaining Small bits of cartilage were free in the joint There was also a distinct roughening of the bone The crucial ligaments were thin and extremely relaxed, and allowed the lateral mobility of the joint The semilunar cartilages were thin and irregular in contour There was a slight fibrous reaction on the sides of the joint

Microscopic examination of a section from the right knee revealed a marked thinning of the femur and thickening of the head of the tibia There was an irregularity of the cartilage which was destroyed in spots along the joint surfaces A marked fibrous tissue reaction was seen in the joint, in which there were clumps of cartilage cells In spots the bone was eroded The semilunar cartilages were present and intact The crucial ligaments were much thinner than normal A sesamoid bone was present in the popliteal space There was a thickening of synovial membrane Pus was not present Slight leukocytic infiltration of the muscle had occurred The surface of the bone gave the impression of one which has healed Small villous processes were present in the joint, which had proliferated from the synovial membrane There was a proliferation of cartilage Little acute inflammation was seen in this joint

and recipient have been in group II. The work of Guthrie and Huck<sup>4</sup> has shown the possibility of a number of groups in addition to the four which are usually considered, but it is doubtful whether it will ever be necessary to give all of these groups practical consideration. However, in the work in our laboratory, we have long recognized two subdivisions of group II, and I believe that they are of practical importance. Attention was first directed to a difference in the behavior of erythrocytes of different group II individuals when it was observed that in some cases agglutination by group III and group IV serum occurred slowly and incompletely. For lack of a better classification, we began to use the terms "slow twos" and "fast twos." The discovery that the percentage of post-transfusion reactions was nearly twice as great when the donor and recipient were in group II as when any other combination was used leads me to believe that the recognition of "strong and weak twos" were of practical importance. At the present time, we are collecting data on the comparative results produced in the form of post-transfusion reactions when both donor and recipient belong to the same subdivision of group II and when the subgroups are mixed. We advocate the preference of group IV or universal donors in all transfusions when no more than 750 cc of blood is to be transfused, especially in selecting professional and semiprofessional donors for group II recipients, because of the existence of subdivisions of group II, which are of practical importance and which increase the incidence of reactions. Besides, as I have pointed out, the only real practical error which might occur in blood grouping by the method employed in our laboratory is when one is dealing with group I individuals and the least possibility of error when one is dealing with group IV individuals. This would argue well for the use of group IV donors with patients of groups I and II at least, group III is such a small group that a group III donor is seldom needed, and when needed is seldom found. I therefore feel justified in recommending the preference for group IV donors in all transfusions when practical.

Two questions frequently asked are whether donating blood is harmful to the donor and whether the group of an individual ever changes. I cannot state positively that the repeated withdrawing of blood in 500 cc quantities is harmful. I have not observed any ill effects. Three of our donors have served between eighty and 150 times over a period of five years, and they are all in excellent health and as far as I know, specimens of fine physique. Some donors cannot

<sup>4</sup> Guthrie, C G and Huck, J G. Existence of More than Four Isoagglutinin Groups in Human Blood. Bull Johns Hopkins Hosp 32 37 (Feb) 1923 34 80 (March) 1923 34 128 (April) 1923

# EXTRAPLEURAL THORACOPLASTY A MUSCLE SPLITTING OPERATION \*

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CHICAGO

The Wilms-Sauerbruch operation of extrapleural thoracoplasty is performed as a routine through a single paravertebral incision. The incision extends from the upper border of the trapezius muscle to a point over the eleventh rib, and is carried down through the layers of muscle to the level of the ribs at the outer border of the erector spinae group.

This incision necessitates transverse section of the trapezius, rhomboids and latissimus dorsi, and is consequently bloody and traumatizing. It is certain that it favors postoperative shock and infection of the wound, complications which, as Archibald has recently brought out, account for most of the direct operative mortality.

Furthermore, when the operation is performed in stages, if even a slight infection occurs after the first or second stage, it is necessary to prolong the interval between operations, frequently to such an extent that the resected ribs regenerate and the final collapse is compromised.

It seemed to me that these drawbacks could be obviated and the function of the arm and shoulder better preserved if the operation were performed through separate incisions and the ribs approached by splitting rather than by transecting the broad muscles of the shoulder girdle.

To meet these requirements, the following muscle splitting operation in three stages has been devised.

The first incision begins over the eleventh rib just lateral to the spine and runs upward and outward over the angle of the scapula. The skin and subcutaneous tissues are freed from the latissimus dorsi for a short distance on each side of the incision, and this muscle is split in the direction of its fibers. The loose areolar tissue binding the muscle to the ribs and the intercostal structures can be freed easily by the finger, and, this having been done, adjustment of the retraction gives easy access to the posterior segments of the eighth, ninth, tenth and eleventh ribs.

The second incision is in the line of the usual paravertebral one and extends from the spine of the scapula to the level of the eighth rib. Small flaps of skin and subcutaneous tissues are dissected up from the trapezius, and the muscle is split in the line of its fibers. The trapezius is freed on its under surface, and the rhomboid is thus brought into view. This muscle is similarly split and freed from the ribs and unde-

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\*From the Surgical Service of the Research and Educational Hospitals of the Medical School of the University of Illinois.

give blood as frequently as others without becoming anemic, but the transfusions apparently do not have any permanent ill effects. In our experience or under our observation the group of an individual has never changed. All apparent instances were found on investigation to have been due to an error in grouping.

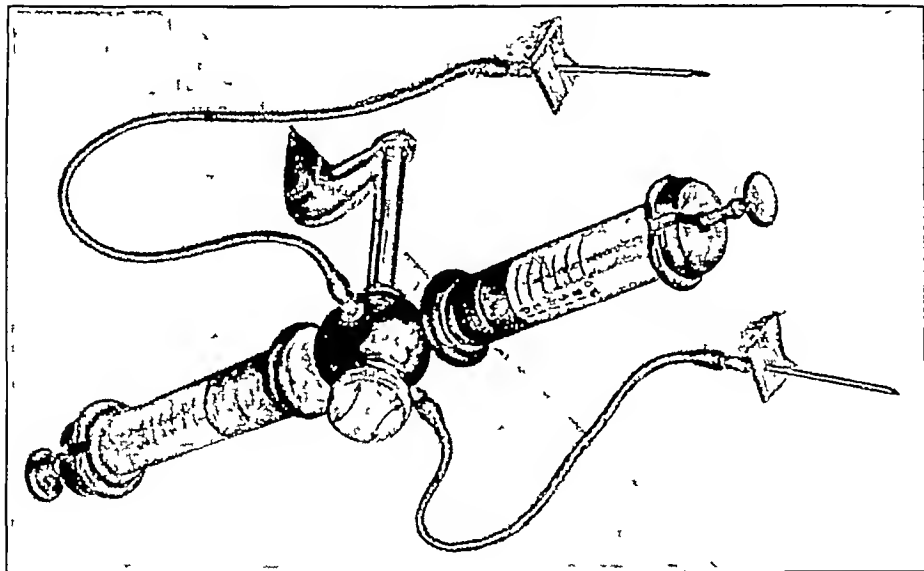


Fig 1—The apparatus used in blood transfusions. The arrows indicate the connections with the circulations of the donor and the recipient

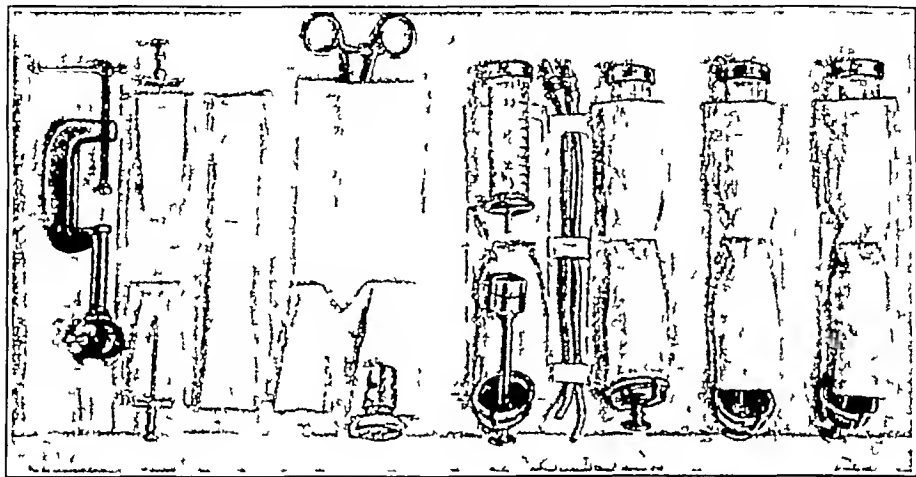
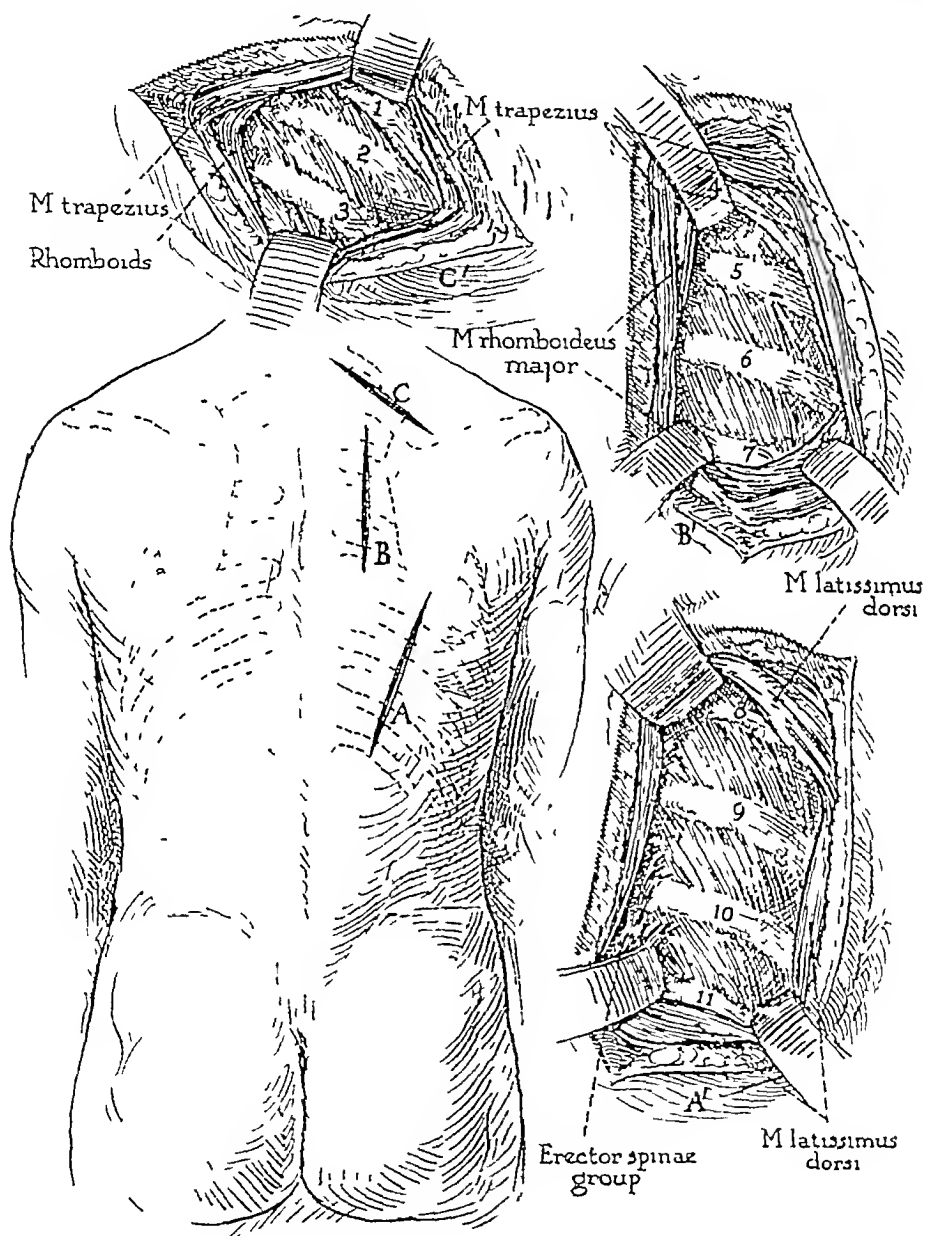


Fig 2—Sections of the apparatus in place in their respective compartments in the canvas roll designed for that purpose

The apparatus which has been used at the Jefferson Clinic and Diagnostic Hospital for the last three years up to a short time ago was a modification described in 1926.<sup>2</sup> This apparatus possessed several minor disadvantages, and we have looked over carefully

lying tissues Adjustment of the retraction gives easy access to the desired segments of the fourth, fifth, sixth and seventh ribs

The third incision is made in the line of the fibers of the trapezius and extends from the second dorsal spine to the middle of the spine of the scapula, or, in case there has not been infection in the second



A muscle splitting operation in three stages for extrapleural thoracoplasty

incision, it may be merely extended upward as has heretofore been the practice Flaps having been raised, the trapezius and rhomboid muscles are split and freed on their under surfaces Then proper adjustment of the retraction affords access to the posterior segments of the first, second and third ribs



the several apparatus placed on the market in the last two years hoping to find one more suitable. All were rejected, however, because of the principle involved or because we believed that our apparatus was more simple, more fool-proof and more accurate. We were not satisfied with any apparatus presented. With these imperfections and undesirable features of the equipment in mind, yet not wishing to make any radical changes or to deviate from the principle involved in the apparatus with which we had performed over 2,000 transfusions, our present apparatus was designed (manufactured by the J. F. Hartz Company, Detroit), the accompanying illustrations of which, I believe, are self-explanatory.

This apparatus possesses the following advantages

Foreign substance is not mixed with the blood, and the blood is not modified in any way

The amount of blood can be accurately measured

The apparatus is small and light and consists of only two parts

Lubrication of moving parts or paraffin coating is unnecessary

Veins are entered by needles

A canvas roll with a separate compartment for every piece of the equipment in which the apparatus can be wrapped immediately after cleaning and autoclaved and in which everything will remain sterile is part of the equipment

By means of arrows, only a glance is necessary to determine whether the operator's syringe communicates with the circulation of the donor or recipient, and thereby is eliminated the possibility of taking blood from or injecting it into the wrong person

By means of two syringes working opposite each other and always connected with the opposite side arm of the apparatus, it is possible to provide a continuous stream of blood from the donor to the recipient and thereby to reduce the possibility of clotting to a minimum, because stagnation will not occur in the apparatus

The donor, or recipient, may be placed on either side of the apparatus

The actual transfusion can be performed in less than five minutes

The blood is not unduly agitated, cooled or exposed to the air

#### METHOD

The donor and recipient are placed in the supine position about 18 inches apart, with their heads in the same direction, their shoulders opposite each other and with a table or board between them in such a position that the elbows of both the donor and the recipient lie over the board at the edge nearest the foot of the table. The donor is placed on the operating table in the operating room, and the recipient is allowed to remain on the stretcher car. An arm board about 12 inches wide is then placed under the pad on the table and allowed to project 18 inches. The car is then brought up to touch the end of the board. In the patient's home, conditions of the operating room must be simulated by various makeshifts

The two patients on whom this operation has been performed were able to be out of bed the third day after the final stage, and could move the arm and shoulder on the affected side freely in all directions without pain

#### SUMMARY

1 The usual paravertebral incision for the operation of extrapleural thoracoplasty has two serious drawbacks

(a) The transverse section of the broad muscles of the back adds to the hemorrhage and trauma and is a factor in postoperative shock, infection and deformity

(b) When the operation is performed in stages, as is usual, infection in one incision necessitates increasing the interval between operations, frequently to such an extent that the resected ribs regenerate and the final collapse is compromised

2 These drawbacks can be obviated by performing the operation in three stages through separate incisions, and by splitting rather than transecting the broad muscles of the shoulder girdle

The arms are bared to the shoulders, and the skin is cleansed with soap and the usual skin antiseptics. Ordinary sterile precautions are observed. Half inch pure gum rubber tourniquets are used, and the pressure of the donor's tourniquet frequently must be varied during the transfusion to obtain the best flow. The patient's tourniquet is removed as soon as the needle is introduced into the vein. The operator stands between the donor and the recipient facing the head of the operating table, and his assistant stands across the board facing him. The operator clamps the apparatus to the side of the board nearest him.

All syringes, which are 20 cc Records, are rinsed with saline. One syringe is filled with saline, and the tip is inserted into the opening on the side nearest the assistant. The apparatus is tested with this saline to eliminate obstruction and to demonstrate to the satisfaction of the operator that the needle is properly placed well within the lumen of the recipient's vein. A small amount of saline is allowed to flow slowly into the recipient's circulation while the needle is being introduced into the donor's vein, and then the remaining saline is discarded. The most prominent veins on the arms of the donor and the recipient are selected, usually these are superficial veins on the ventral surface of the arm over the elbow joint, but frequently other veins of the forearm and occasionally the radial veins are preferable. In the case of the donor, a deeper seated, well anchored vein is to be preferred to the easily movable, readily collapsed, superficial vein. Needles are inserted "toward the heart" because it is easier to introduce needles placed in this direction. The slight advantage in placing the donor's needle "toward the hand" does not compensate for the added difficulties encountered.

The skin is pierced beside the vein first, and then the vein is entered with a separate, slow, purposeful movement. Do not "peck" or "jab" at a vein. It is best to have about two thirds of the length of the needle buried beneath the skin. Needles must be sharpened before each transfusion. This is imperative. Fairly long concave bevels are best. We "hollow-grind" our needles by use of a small motor-driven emery wheel which is supplied at small cost by all firms that sell laboratory supplies. A 15 gage needle is used for the recipient and a 13 gage needle for the donor. The rubber tubing should have thick, stiff walls, cut in 9 inch lengths and a lumen that is just large enough to admit the adaptors. When the needles are in position, the donor's syringe is first filled with blood from the donor, then the stopcock is reversed, and this blood is emptied into the recipient's circulation while the assistant fills his syringe with donor's blood. This procedure is repeated until a sufficient amount has been transferred.

In the majority of transfusions, 500 cc can be given with the same two syringes. Occasionally, they begin to stick before the transfusion is completed, and it is necessary to exchange them for fresh ones, more than one change is rarely necessary. No less than four syringes should constitute a set. A slight amount of "sticking" is sometimes encountered which lasts while two or three syringes are being taken, and which is eliminated if additional strength is exerted when the plunger is pulled or pushed.

Either or any other substance should not be used to prevent "sticking" of the plungers. Speed in filling and emptying syringes is important for the success of the transfusion.

# AN EXPERIMENT WITH BROTH CULTURES OF STAPHYLOCOCCUS AUREUS AND GENTIAN VIOLET \*

A R SHANDS, JR, M D  
WASHINGTON, D C

Following the lines of experimentation of Churchman <sup>1</sup> in 1922, when he showed that a slight increase in temperature had a definite effect on the bacteriostatic power of gentian violet, and of Gatch, Trusler, and Owen <sup>2</sup> in 1925, when they showed that gentian violet in 4 per cent dextrose was less toxic for rabbits than aqueous gentian violet, experiments were performed in test tubes and on agar plates to correlate these facts

Twenty-four hour broth cultures of *Staphylococcus aureus* containing about 9 cc of fluid were used Gentian violet was prepared first

*Reaction of Staphylococcus aureus Broth Culture to Aqueous and 0.25  
Per Cent Dextrose Gentian Violet in the Incubator at 37.5 C  
and in the Water Bath at 50 C \**

	0 Min	2 Min	4 Min	6 Min	8 Min	10 Min	15 Min	20 Min	30 Min	40 Min	60 Min	120 Min
I Incubator 37.5 C												
1 Control	+	+	+	+	+	+	+	+	+	+	+	+
2 Aqueous gentian	+	+	+	+	+	+	+	+	+	+	+	+
3 Dextrose gentian	+	+	+	+	—	—	—	—	—	—	—	—
II Water bath 50 C												
1 Control	+	+	+	+	+	+	+	+	+	+	+	—
2 Aqueous gentian	+	+	+	+	+	+	+	+	+	+	+	—
3 Dextrose gentian	+	+	—	—	—	—	—	—	—	—	—	—

\* Dilution of gentian violet, 1 to 10,000

with distilled water as a medium and then with 4 per cent dextrose as a medium Sufficient amounts of the gentian violet preparations were added to the broth cultures to make a 1:10,000 dilution of the dye A bath at 50 C was used to give the increase in temperature A series of six broth cultures was used, divided as follows two contained aqueous gentian violet, two 4 per cent dextrose gentian violet, and two controls One set of three cultures was placed in the incubator at 37.5 C and one set in the water bath at 30 C Subcultures were taken immediately before adding the gentian violet, and at periods thereafter of five, ten, fifteen, twenty, thirty, forty, sixty minutes, and two hours

\*From the Louis Bowles Foundation of the Children's Hospital School, Baltimore

1 Churchman, J W Bull Johns Hopkins Hosp 33 277 (June) 1922

2 Gatch, W D, Trusler, H M, and Owen, J E Treatment of General Septicemia by Gentian Violet and Mercurochrome-220 Soluble, J A M A 85 894 (Sept 19) 1925

When the transfusion is finished, the operator should clean the apparatus. It should be placed in the cover, rolled up and sterilized in the autoclave immediately at 5 pounds' pressure for ten minutes. A convenient method is to autoclave the set under the same conditions observed for rubber gloves. Thus a sterile apparatus is always ready. A lubricant or coating should not be used for any part of the apparatus, and a new rubber tubing should be used for each transfusion. The apparatus can be used satisfactorily by one person if an assistant is not available. In that case the assistant's syringe is left in position but is disregarded when the transfusion has been started. Of course, an assistant is desirable to provide a steady flow of blood.

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Plain agar plates were used for the subcultures. The cultures were noted in twenty-four and forty-eight hours. In the incubator the cultures did not show any growth in the aqueous gentian violet after sixty minutes, nor any growth in the 4 per cent dextrose gentian violet after five minutes. In the water bath there was no growth at any period in either the aqueous or 4 per cent dextrose gentian violet cultures, nor was there a growth in the control culture after sixty minutes. The experiment was now checked and the results obtained, except that in the water bath the aqueous gentian violet showed a growth at five minutes. An attempt was made to determine more nearly the time the cultures became sterile. The same experiment was repeated with subcultures made at two, four, six, eight, ten, fifteen and twenty minute intervals after the addition of the gentian violet. In the incubator there was no growth after six minutes in the 4 per cent dextrose gentian violet, while the aqueous gentian violet showed a growth in all cultures. In the water bath there was no growth after six minutes in the aqueous gentian violet, and no growth after two minutes in the 4 per cent dextrose gentian violet.

From this experiment it is concluded that dextrose gentian violet is more toxic for *Staphylococcus aureus* than aqueous gentian violet, and that heat has a definite effect on the bactericidal power of the gentian violet. *Staphylococcus aureus* is therefore destroyed quicker by gentian violet in 4 per cent dextroses than in sterile water, and in the presence of an increase in the surrounding temperature.

# STUDIES IN INTESTINAL OBSTRUCTION

II THE ABSORPTION OF HISTAMINE FROM THE OBSTRUCTED BOWEL \*

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AND

MILO LOUCKS, PH.D.

MINNEAPOLIS

In intestinal obstruction, the factor of absorption from the bowel is uniformly acknowledged as being of the greatest importance. It is generally stated that with the stretching and damaging of the wall of the bowel incident to distention by obstruction, absorption of the toxic material from the bowel occurs to which the mucous membrane of the normal bowel is impermeable.

It has been adequately demonstrated that the obstructed bowel permits the absorption of substances from its lumen to which the normal bowel is permeable. Braun and Boruta<sup>1</sup> have been able to show that strychnine is absorbed from the obstructed intestine of the dog, but at a slower rate than from the normal intestine. Clairmont and Ranz<sup>2</sup> found that potassium iodide was absorbed from the obstructed intestine of the dog more rapidly during the first ten hours following the obstruction than from the normal bowel. From ten to fifteen hours after the obstruction, the absorption became reduced in amount and quickly sank to a low level. Enderlen and Hotz<sup>3</sup> observed that the absorption of various concentrations of saline and dextrose in the obstructed intestine of the dog was retarded from the start, some time following the establishment of the obstruction, the absorption from the obstructed bowel was slight. Later during obstruction they observed an exudation of fluid into the bowel. Enderlen and Hotz<sup>3</sup> stated that in the animal with intestinal obstruction, the absorption from the nonobstructed segments is also diminished. In contrast to the greatly changed external appearance of the bowel in strangulation obstruction, Enderlen and Hotz found that there was little change from the normal bowel in the absorption of varying con-

\* From the Departments of Surgery and Physiology of the University of Minnesota

\* Presented before the Minnesota Pathological Society, April 19, 1927

1 Braun, W., and Boruta, H. Experimental kritische Untersuchungen ueber den Ileus Tod, Deutsche Ztschr f Chir 96 544, 1908  
 2 Clairmont F., and Ranz, E. Zur Frage der Autointoxication bei Ileus, Arch f klin Chir 73 696, 1904  
 3 Enderlen and Hotz Ueber die Resorption bei Ileus and Peritonitis, Mitt a d Grenzgeb d Med u Chir 23 755, 1911

The remaining sixty-three cases (58 per cent) formed a third group which was distinct from the other two in that the palpable nodules or tumors of the thyroid glands were composed of sharply localized areas of hypertrophy and hyperplasia while the intervening parenchyma of the thyroid presented the microscopic structure of a normal gland. In these cases, the morbid process had remained confined to certain localized, well defined areas of the gland instead of spreading diffusely throughout the thyroid as in the two groups of cases already described. The clinical histories in these cases revealed a low grade hyperthyroidism of long standing, with a relatively chronic course which manifested



Fig. 25—Photograph of paraffin block of right lobe of thyroid removed from patient, aged 63, with basal metabolic rate of plus 60. Nodular fibillation and a long history of hyperthyroidism. Specimen originally the size of 3 mm. x 1 mm. x 1 mm. but fixing in formaldehyde caused a great deal of shrinkage. The large nodules at top of the picture are areas of hyperplastic parenchyma. The large tumor occupying the greater part of the lobe was a white gray mass of fibrous tissue cellular detritus, fat and a homogeneous mass. The tumor is outlined by flattened normal thyroid parenchyma. The isthmus and left lobe of the thyroid in this case were normal in appearance and a piece removed from each showed a normal microscopic picture. The patient improved after removal of the right lobe. She now has a normal basal metabolic rate and a normal heart rhythm. Reduced to one-half its actual size.

itself more prominently in the fourth fifth and sixth decades. Clinically and in the gross specimens the tumors or nodules of the thyroid were readily palpable and varied in size from small shothike nodules



to tumefactions the size of a man's fist or even larger (fig 25) In the gross specimen on section these nodules formed sharply circumscribed areas with an apparent encapsulation, the thickness of which was usually proportionate to the duration of the disease and the age of the patient (fig 17) These tumors appeared to be composed of parenchymatous tissue and toward the center often contained small cysts or bluish-white stellate areas of connective tissue Microscopically, these nodules were seen to be composed of thyroid parenchyma in a state of hypertrophy and hyperplasia similar in all respects to that<sup>1</sup> observed throughout the gland as a whole in cases of exophthalmic goiter (figs 21, 26, 27 and 28) In the majority, the acini appeared to be larger

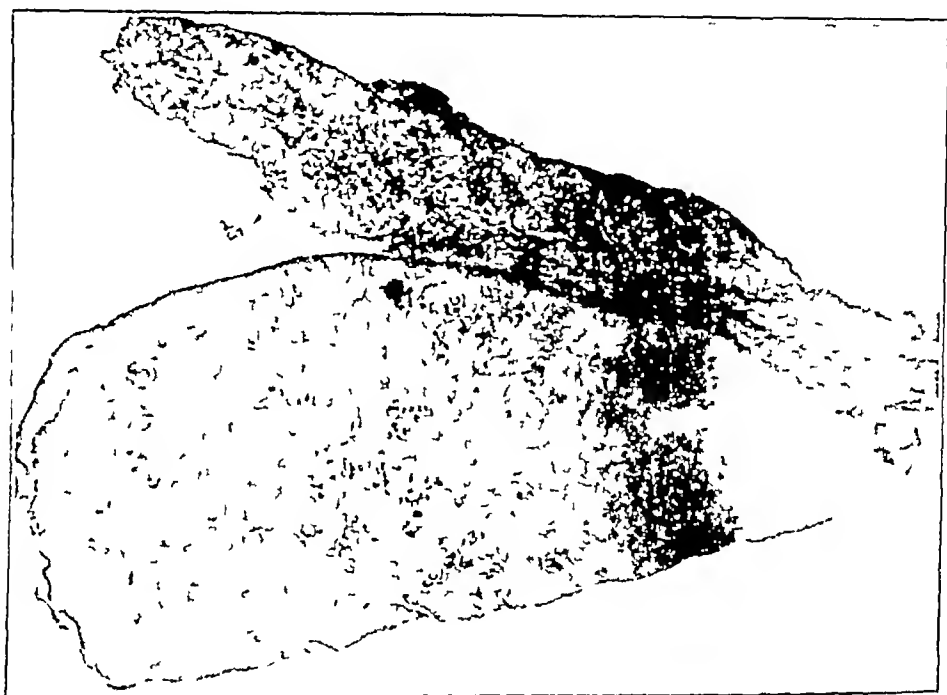


Fig 26—Low power photomicrograph of a tumor the size of a golf ball removed from the thyroid gland of a patient with hyperthyroidism In the upper portion of the section there is a spur of contiguous normal thyroid parenchyma removed with the tumor Reduced from a magnification of  $\times 8$

and of the lacelike type with the characteristic papillomatous infoldings (figs 22 and 29), yet in some the nodules were composed of a greater number of small, round acini, while in others both types of hyperplasia were noted (figs 30 and 31) The epithelium lining these acini showed the characteristic histologic changes associated with an increased functional activity of the cells—columnar shape, vacuolated cytoplasm with an increase in the mitochondria and vesicular, clear-staining nuclei Vacuolization was present in the colloid, which seemed less viscid than normal and stained poorly In the majority of cases, the hyperplastic and hypertrophic parenchyma was characteristic and in the best state

centrations of dextrose and saline Braeye,<sup>4</sup> in studying the passage of toxins obtained from an obstructed bowel through an isolated obstructed loop, was unable to determine any abnormal absorption with soap solution

The nature of the toxin in intestinal obstruction is a disputed point even among those who generally accept the absorption of an intestinal toxin as the cause of death Every one agrees, however, that if there is a toxin in the bowel of the animal in which intestinal obstruction has been produced which is not present in the intestine of the normal animal, the toxin has its source above the point of obstruction and probably takes origin in protein disintegration

In this study, histamine was placed in the intestine of both the normal dog and the dog with intestinal obstruction, and acute experiments were performed to test for the physiologic action of histamine as observed in the blood pressure Gerard<sup>5</sup> stated that the toxic substance in intestinal obstruction actually is histamine It is known, however, that histamine is present in the bowel of both man and the normal dog<sup>6</sup> and also in the bowel of the dog with intestinal obstruction<sup>7</sup> The eliciting of the physiologic test for histamine when injected into the bowel of the dog with intestinal obstruction would adduce convincing proof that the bowel of the animal was permeable to toxic substances which the normal bowel did not allow to pass

#### METHOD

Blood pressure tracings were recorded by a kymograph from the carotid artery of the dog under ether anesthesia After the pressure level had been established, the abdomen was opened, and the pressure level was again allowed to adjust itself following the transitory change that occasionally occurred when the abdomen was opened or a loop of bowel was raised Histamine dichloride was then injected into the

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4 Braeye, Louis Contribution to the Study of Toxic Absorption from the Intestinal Tract in Experimental High Obstruction, *Bull Johns Hopkins Hosp* **40** 33, 1927

5 Gerard, R. W Chemical Studies on Intestinal Intoxication, The Presence and Significance of Histamine in an Obstructed Bowel, *J Biol Chem* **52** 116, 1922, The Lethal Agent in Acute Intestinal Obstruction, *J A M A* **79** 1581 (Nov 4) 1922

6 Hanke, M T, and Koessler, K K Studies on Proteinogenous Amines, On the Presence of Histamine in the Mammalian Organism, *J Biol Chem* **59** 879, 1924 Meakins, J, and Harington, C R The Relation of Histamine to Intestinal Intoxication, I The Presence of Histamine in the Human Intestine, *J Pharmacol & Exper Therap* **18** 455, 1921 Mellanby An Experimental Investigation on Diarrhea and Vomiting of Children, *Quart J Med* **9** 165, 1916

7 Gerard R W (footnote 5, second reference)

of mercury and then by a gradual decline to 50 mm. at 3 30 The ligature was again loosened, and the pressure continued to fall At 3 35 the pressure was 30 mm Seven cubic centimeters of intestinal contents was now aspirated from the strangulated loop and injected into a mesenteric vein with a gradual decrease of pressure The dog died at 3 50

*Summary*—Strangulated obstruction of two hours' duration was established A marked fall in pressure occurred when the constriction was released When the ligature was tightened, a short rise in pressure occurred

EXPERIMENT 19 (dog 89)—Dec 30, 1926 Strangulated obstruction of a loop of the lower part of the ileum, together with its mesentery was performed under aseptic technique at 11 30 a m A carotid artery tracing was started at 2 p m under ether anesthesia The tracing from this experiment has also been lost, so that only the protocol written at the time is available, consequently, definite figures as to arterial pressure at any time cannot be given At the beginning of this experiment, the pressure was good At 2 05, the abdomen was opened without much effect on the pressure The bowel was only moderately cyanotic and rather thickened on palpation At 2 20, the ligature about the bowel and mesentery was loosened, with an immediate fall in pressure At 2 35, the ligature was tightened, and the pressure rose gradually At 2 50, the ligature was loosened again, and a slight but definite fall in the arterial pressure occurred Fifty milligrams of histamine was injected into the strangulated bowel at this time, apparently without direct effect on the pressure At 3 10, a portion of the contents into which the histamine had been injected was aspirated from the loop and injected into a mesenteric vein, causing a great fall in pressure

*Summary*—A strangulated obstruction was established for two and one-half hours Release of the constriction was attended by a fall in pressure On tightening the ligature, the pressure rose

EXPERIMENT 20 (dog 90A)—Dec 31, 1926 Aseptic strangulated gut obstruction was produced at 11 30 a m by tying off a loop of the ileum and mesentery about 5 feet (152.4 cm) in length The bowel was then irrigated with a solution of 10 per cent formaldehyde, ether and alcohol until the contents returned clear The dog was again anesthetized A tracing was started at 2 50 p m The dog was extremely ill The blood pressure at the beginning of the experiment was 118 mm of mercury, but fell gradually At 2 58, the abdomen was opened The arterial pressure went down to 90 mm of mercury The strangulated loop was raised The blood pressure at 3 10 was 50 mm and at 3 15, 48 mm The ligature was detached from the bowel and mesentery The blood pressure continued to fall at the same rate, and at 3 25 had dropped to 40 mm At 4, 10 mg of histamine was injected into a mesenteric vein, death followed

*Summary*—Strangulation obstruction of the intestine was established and maintained for three and one-half hours The pressure was low at the beginning of the experiment The dog was in a state of shock Release of ligature was accompanied by a continued decline in pressure

EXPERIMENT 21 (dog 92)—Dec 3, 1927 Strangulated obstruction of 5 feet or the bowel was established at 5 p m by tying off the bowel loop and mesentery with a gauze under aseptic technique The bowel was irrigated with 10 per cent formaldehyde, ether and alcohol until the contents returned clear The dog was anesthetized again with ether at 7 30 A tracing was begun at 7 42, the pressure being 210 mm of mercury (fig 7) The abdomen was opened at 7 50 The

lumen of the bowel with a fine hypodermic needle. This procedure was first carried out in the normal, and then in the obstructed ileum and duodenum. Blood pressure tracings were also obtained in a few dogs in which duodenal obstruction had been created two days previously without injecting histamine into the obstructed bowel at the time the observations on the blood pressure were made. A number of tracings were made on dogs in which strangulation obstruction had been established a few hours previously. In some of these experiments, histamine was injected into the bowel before the strangulating mechanism was released, in others, the introduction of histamine into the bowel was omitted.

In a few of the early experiments the tracings were made under a combination of morphine and local anesthesia, and the pressure was obtained from the femoral artery. In most of the tracings, however, ether anesthesia was employed, and the pressure was recorded from the carotid artery. Unless otherwise specified, it is implied that the blood pressure was registered from the carotid artery and that ether anesthesia was used. Whenever the intestines were obstructed by operation quite an interval prior to the time that the tracing was made, aseptic technic was employed, and the animals were allowed to recover from the anesthetic before the second procedure was begun. Severed gut obstructions were established by cutting across the bowel and inverting the ends. Strangulation obstructions were created by placing a gauze ligature around a loop of bowel, from 3 to 5 feet (91.44 to 152.4 cm) in length, together with its mesentery. The degree of constriction obtained by the ligature was varied. In a few instances in which complete cessation of blood flow was desired, Carmalt noncrushing clamps were placed across the mesentery. In this study, pressure readings were made on twenty-eight dogs.

#### EXPERIMENTS

EXPERIMENT 1 (dog 71) —Nov 27, 1926. Absorption of histamine from the normal duodenum.

A tracing was made on a large female collie with a cannula in the right femoral artery under ether anesthesia at 12.40 p. m. The blood pressure at the beginning of the tracing was 124 mm of mercury. The abdomen was opened and the duodenum isolated by clamping off a segment about 8 inches (20.3 cm) in length with intestinal clamps cross the bowel. At 1.10, 10 mg of histamine was injected into the femoral vein with only a slightly perceptible change in the arterial pressure. At 1.20, 10 mg of histamine was injected into a mesenteric vein with an immediate depression of the pressure to 75 mm of mercury. At 1.40, the blood pressure had risen to 90 mm of mercury. Ten milligrams of histamine was then injected into the femoral vein with a drop in pressure to 50 mm of mercury. After twenty minutes, the pressure rose to 90 mm of mercury, and 50 mg of histamine and enough water to make the obstructed loop of the intestine tense, was injected into it. Change in the

arterial pressure was 200 mm. The strangulated loop was moderately cyanotic and discolored with some free hemorrhagic fluid present in the peritoneal cavity. The strangulated loop was carefully delivered and isolated in warm saline packs placed on the abdominal wall. At 8 10 the pressure was 180 mm of mercury. The ligature about the bowel and the mesentery was loosened at 8 13, with an almost immediate fall in pressure to 140 mm. The vessels to the strangulated bowel were soon pulsating, and at 8 20, the normal luster had returned to the strangulated loop, and the pressure was 132 mm of mercury. At 8 35, the pressure had fallen to 104 mm. The ligature on the intestine was tightened again. Ten minutes later, at 8 45, the bowel was again moderately cyanotic. The pressure had risen to 110 mm. At 8 55, the pressure remained unchanged, at 9 05, the pressure had arisen to 118 mm, and the constriction on the bowel and the mesentery was loosened again. At 9 10, the color had returned to the bowel, and the vessels were pulsating. The pressure had fallen to 100 mm, and at 9 25 had dropped to 80 mm. Twenty cubic centimeters of intestinal contents was then aspirated from a normal loop, diluted with a little saline solution and injected into a mesenteric vein. The arterial pressure had continued to fall and was then 54 mm. Ten minutes later, the dog was dead.

*Summary*—A strangulated obstruction was established and had been maintained for three and one-half hours. The pressure was good when the tracing was started. A release of the constriction was attended by a sudden primary and gradual reduction of pressure. When the ligature was tightened the pressure rose

EXPERIMENT 22 (dog 140)—March 8, 1927. A large collie was used in this experiment. The tracing was started at 10 40 a m. The blood pressure was 200 mm of mercury. The abdomen was opened at 10 50. At 10 55, the mesentery to a loop of the midileum, about 3 feet in length, was clamped off with two Carmalt hemostatic forceps so as completely to deprive this segment of its blood supply. At 12 20, one hour and twenty-five minutes later, the two clamps were released without any alteration in pressure. At 1 25, the blood pressure was unchanged. Air was injected into the left ventricle, death resulted.

*Summary*—Strangulation of a loop of the intestine was established at the time of operation. Release of the ligature one hour and twenty-five minutes later did not show a fall in pressure.

EXPERIMENT 23 (dog 145)—April 13, 1927. A loop of the intestine was strangulated for 30 inches (76.2 cm) by placing clamps on the mesentery at 10 30 a m. A tracing was started at 4 23 p m under ether anesthesia, the clamps were removed at 4 43 (fig. 8). The bowel was markedly discolored. From the time the clamps were loosened, the pressure gradually fell. About twenty-five minutes after loosening the clamps, the bowel was regaining luster, but the blood pressure continued to decrease, and the dog died at 5 53, one hour and ten minutes after the removal of the clamps. The pressure at the beginning of the tracing was 150 mm, at 4 36, just after opening the abdomen, 132 mm, at 4 43, when the clamp was loosened, 140 mm, ten minutes after loosening the clamp, 100 mm, at 5 03, 84 mm, at 5 13, 75 mm, at 5 23, 60 mm, at 5 33, 50 mm, at 5 43, 40 mm, and at 5 50, 20 mm. Death occurred at 5 53.

*Summary*—A strangulation obstruction was established and maintained for six hours. The pressure was good at the beginning of the experiment. After the clamps were released, there was a gradual reduction in pressure followed by death in one hour and ten minutes.

EXPERIMENT 24 (dog 146)—April 16, 1927. Strangulation obstruction of the intestine was established at 10 30 a m by ligating 4 feet of the midileum. A

blood pressure did not occur over a half hour period. Ten milligrams of histamine was then injected into a mesenteric vein with an immediate reduction of pressure to 44 mm, death resulted.

*Summary*—A physiologic effect was obtained when histamine was injected intravenously into the systemic and into the mesenteric veins. The injection of 50 mg of histamine into the duodenal loop which had been made tense by distending it with water did not have any effect.

EXPERIMENT 2 (dog 79)—Dec 20, 1926 Absorption of histamine from the normal ileum

A tracing was started at 10 17 a m (fig 1). The arterial pressure was 140 mm. At 10 34, the abdomen was opened, the pressure being 150 mm. At 10 48, rubber covered clamps were applied 3 feet apart across the lower part of the ileum. At 10 55, the pressure was 130 mm. At 10 57, 50 mg of histamine and enough water to make the loop distended was injected into the intestine with a fine hypodermic needle. At 11 07, the arterial pressure was 128 mm. The pressure continued at the same level. At 12 04 p m, one hour and nine minutes following the injection of the histamine into the lower ileal loop, the pressure was still unchanged. Ten milligrams of histamine was then injected into a mesenteric vein with an immediate fall of pressure to 70 mm. At 12 09, 1 cc. was aspirated from the loop into which the histamine had been injected, with a quick fall in pressure to 56 mm, followed by a progressive decline. The dog was killed with ether.

*Summary*—A fall in pressure did not occur after one hour and nine minutes following the injection of 50 mg of histamine into the normal loop of the ileum.

EXPERIMENT 3 (dog 80)—Dec 20, 1926 Aseptic gut obstruction (lower part of the ileum) was established at 11 a m

A tracing was started December 21, at 3 06 p m. The arterial pressure was 110 mm of mercury. The abdomen was opened at 3 12, and six minutes later the arterial pressure was 136 mm. A rubber covered clamp was applied across the bowel about 18 inches (45.7 cm) proximal to the obstruction in the ileum. The blood pressure at 3 25 was 130 mm of mercury. At 3 26, 50 mg of histamine was injected into the obstructed loop. At 3 32, the blood pressure was the same. At 3 45, 3 54 and 4 07, the systolic pressure was 130 mm. At 4 17 the blood pressure was 124 mm of mercury. At 4 30, the blood pressure dropped to 118 mm of mercury, and 25 mg more of histamine was injected into the obstructed loop. At 4 45, the blood pressure was 110 mm, at 4 57, it remained the same. Three cubic centimeters of contents from the obstructed loop containing histamine was then injected into a mesenteric vein with an immediate fall in pressure to 56 mm. At 5 03, the blood pressure had gradually returned to 80 mm. Three cubic centimeters of intestinal contents was then aspirated from the colon and injected without effect. At 5 15, the blood pressure was 70 mm of mercury. Three cubic centimeters were aspirated from the obstructed loop containing histamine and injected into a mesenteric vein with a fall to 40 mm of mercury. Air was injected into the heart, death resulted.

*Summary*—A fall in pressure did not occur in one hour in the dog with severed ileal gut obstruction of twenty-four hours' duration after 50 mg of histamine was placed in the bowel.

EXPERIMENT 4 (dog 72)—Nov 30, 1926 Aseptic severed duodenal gut obstruction was established at 11 a m

On December 1, at 11 55 a m, a tracing was started under procaine hydrochloride anesthesia from the right femoral vein of the abdominal wall after a

tracing was started at 1 48 p m. The blood pressure was 160 mm of mercury. The abdomen was opened at 1 50 and the ligated loop was found to be very dark. The strangulated loop was opened near one end, and as much of the material in the lumen as possible was pressed out, following this, the loop was irrigated with water until the contents, although slightly hemorrhagic in appearance, returned fairly clear. The blood pressure was 160 mm of mercury. At 2 02, the obstructing mechanism was released, and the pressure promptly fell to 130 mm of mercury. At 2 05, the clasper was returning to the bowel, and the vessels were pulsating. The pressure had fallen to 108 mm of mercury. Following this, there was a gradual rise to 130 mm of mercury at 2 10, with a fall at 2 12 to 98 mm of mercury. At 2 15, the blood pressure had risen to 130 mm of mercury, and was apparently sustaining itself at this level. The contents that had previously been aspirated were replaced in the bowel at 2 20 without any effect on the pressure. At 2 22, the blood pressure was 124 mm of mercury. At 2 24, 15 mm of histamine was injected into the bowel without apparent effect. The constricting mechanism at this time was tightened, and the blood pressure rose at 2 45 to 140 mm of mercury. At 2 49, the constricting mechanism was released, and the pressure promptly fell to 110 mm of mercury. At 2 55, some of the contents were aspirated from the strangulated loop and injected into the mesenteric vein, this was followed by a prompt fall in pressure to 50 mm of mercury, death then occurred.

*Summary*—A strangulation obstruction of the gut was established and maintained for three and one-half hours. Release of the constriction was accompanied by a sharp and definite fall of arterial pressure, even after the contents of the obstructed bowel were washed out. When the constriction was again placed about the bowel and the mesentery, the pressure rose. Release of the strangulating mechanism was again accompanied by a decided fall in pressure. Neither the replacement of the removed intestinal contents in the bowel nor the injection of 15 mg of histamine into the strangulated bowel accelerated the fall in pressure.

EXPERIMENT 25 (dog 114)—Feb 3, 1927. A tracing from the carotid artery was started at 3 40 p m under ether anesthesia. The pressure was 230 mm of mercury. The abdomen was opened at 3 55. At 4 10, 4 cc. of peritoneal fluid from a dog with a strangulated gut obstruction<sup>2</sup> was injected into the mesenteric vein with only a slight and transient fall in arterial pressure. At 4 23 another injection of 4 cc was made with the same result. At 4 32, 15 cc. was injected with a more definite but transient fall of pressure to 176 mm of mercury. At 4 50, the blood pressure was 200 mm. Fifteen milligrams of histamine was now injected into a mesenteric vein, resulting in a sudden and sustained fall to 130 mm. At 5 15 death was produced by asphyxia.

*Summary*—A slight and transient fall of pressure occurred after the injection of peritoneal fluid from an autolyzed loop of the intestine into the mesenteric vein of the dog. Sustained reduction was produced by the injection of 15 mg of histamine into the mesenteric vein.

8 The origin of the fluid is as follows. A piece of midileum about 12 inches (30.48 cm) in length weighing 73 Gm was removed from one dog and placed in the peritoneal cavity of another after the bowel was irrigated until the contents returned clear. This segment of the bowel was then opened along the antimesenteric border, and the mucosa was washed and scrubbed. When the dog into the peritoneal cavity of which this loop was placed died, two days later, this hemorrhagic fluid was obtained for injection.

previous subcutaneous injection of 240 mg of morphine sulphate, pressure at this time was 154 mm of mercury. At 11 58, the abdomen was opened. The pressure remained unchanged. At 12 00, 100 mg of histamine was injected into the obstructed duodenal loop. A rubber covered intestinal clamp was applied across the gut at the pylorus. At 12 15 p m, the pressure was still 154 mm of mercury. At 12 17, a clot was removed from the vessel, following which there was a fall in pressure to 120 mm of mercury. At 12 22, another clot was removed from the vessel, the pressure, meanwhile, having fallen to 80 mm of mercury. At 12 32, the histamine was removed from the bowel by aspiration, without any change in pressure. At 12 47, one fourth of the material removed

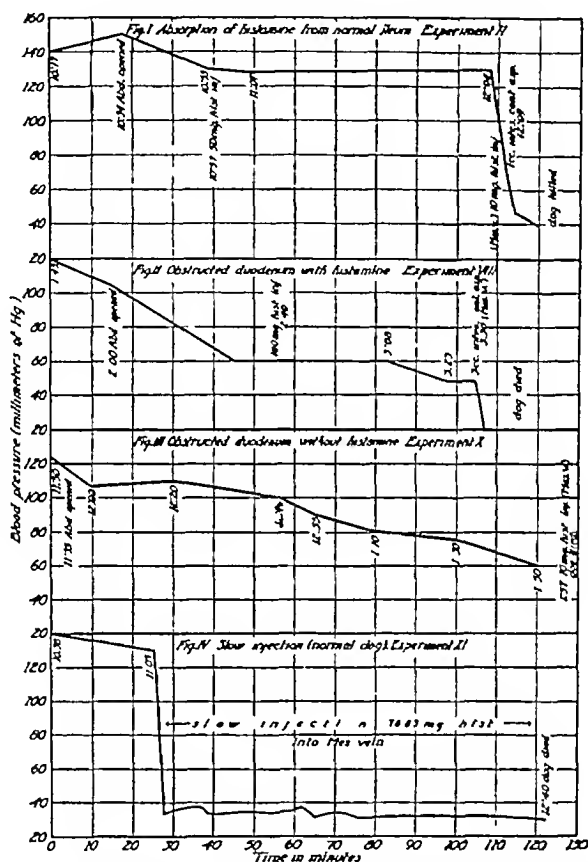


Chart 1—Figure 1, experiment 2, is the blood pressure curve showing that the placing of histamine in the normal ileum did not cause any effect, figure 2, experiment 8, blood pressure tracing showing the effect of placing histamine in the obstructed duodenum, figure 3, experiment 10, blood pressure tracing showing the effect of obstruction without injecting histamine in the bowel, and figure 4, experiment 11, blood pressure tracing showing the effect of extremely slow injection of histamine intravenously

from the loop was injected into a mesenteric vein, causing an immediate drop in pressure almost to the base line, death followed at 12 58

**Summary**—A gradual fall of pressure occurred after the introduction of 100 mg of histamine into the duodenal loop of a dog with a two day severed gut duodenal obstruction



EXPERIMENT 26 (dog 133)—Feb 21, 1927 An aseptic ligation of the aorta and vena cava was performed above the bifurcation with gauze at 12 45 p m, and ileolumbar vessels on each side were also ligated to diminish peripheral anastomosis. When the dog was anesthetized again, he could not stand up, owing to the anemia and consequent paralysis of the hind extremities. A tracing was started at 3 30 p m. The blood pressure at this time was 200 mm of mercury. At 3 45, the ligature was removed from the aorta without effecting a change in pressure. At 3 50, the ligature was removed from the vena cava without any change in the blood pressure for over an hour.

*Summary*—A ligation of the aorta and the vena cava was performed. Three hours later, there was no reduction in blood pressure following release of the constriction.

EXPERIMENT 27 (dog 135)—Feb 28, 1927 At 11 00 a m, a Carmalt clamp was applied across the splenic pedicle and another across the right renal vessels of a dog. A tracing was begun at 3 20 p m with the cannula in the right carotid artery. The blood pressure was 240 mm of mercury. The abdomen was opened at 3 25, and the spleen was found to be bluish and soft with free hemorrhagic fluid in the peritoneal cavity. At 3 40, the clamp was removed from the splenic vessels. Red spots began to appear on the external surface of the spleen, and the organ became firm in consistency. At 3 55, the blood pressure was 190 mm of mercury. At 4 05, the clamp was removed from the pedicle of the right kidney without any change in pressure. At 4 25, when the tracing was discontinued, the blood pressure remained at 190 mm of mercury.

*Summary*—A moderate fall in pressure occurred following the release of the clamp on the splenic pedicle which had been placed there more than four hours previously. When the clamp placed on renal pedicle five hours previously was released, a fall in pressure did not occur.

EXPERIMENT 28 (dog 136)—March 5, 1927 A tracing was started at 3 40. The blood pressure was 250 mm of mercury. At 3 50, 50 mg of histamine was injected subcutaneously over the wall of the chest. There was a gradual but definite fall of pressure to 200 mm of mercury at 3 52. At 4 o'clock, the blood pressure had dropped to 170 mm of mercury. Fifty milligrams more of histamine was injected subcutaneously over the wall of the chest. The blood pressure at 4 01, was 160 mm of mercury. At 4 05, it had fallen to 150 mm. The pressure was maintained at this level, and the experiment was discontinued.

*Summary*—A definite fall of pressure occurred following subcutaneous injection of histamine.

## SUMMARY

When from 50 to 100 mg of histamine was placed in the duodenum or ileum of normal dogs, a fall in pressure was not observed in any of the four animals for a period of an hour or more following the introduction of the drug. The injection of from 3 to 10 mg of histamine into a mesenteric vein was always followed by a sharp fall in pressure. When a few cubic centimeters of the intestinal contents were aspirated from the loops of the bowel into which histamine had been introduced and were injected into a mesenteric vein, there was a sudden fall in arterial pressure, which characterized the histamine reaction.

In a dog with a severed gut obstruction in the lower part of the ileum of thirty hours' duration, the arterial pressure after the introduction of

EXPERIMENT 5 (dog 73) —Dec 2, 1926 Aseptic severed gut duodenal obstruction was established at 10 30 a m

At 12 06 p m, a tracing was started under morphine and procaine hydrochloride anesthesia of the abdominal wall, the dog having thirty minutes previously been injected hypodermically with 140 mg of morphine. The blood pressure at this time was 140 mm of mercury. The abdomen was opened at 12 10. At 12 13, 100 mg of histamine was injected into the obstructed duodenal loop. The blood pressure was 118 mm of mercury. At 2 25, the blood pressure was unchanged. At 12 38, the anesthesia proved insufficient and ether was administered. At 12 50, 80 mg of morphine was again given hypodermically in an endeavor to carry on the experiment without ether. At 1 o'clock, the blood pressure was 80 mm of mercury and the experiment was discontinued because of unsatisfactory anesthesia.

EXPERIMENT 6 (dog 74) —Dec. 6, 1926 Aseptic severed duodenal obstruction was established at 2 30 p m

A tracing was started under ether anesthesia (no morphine) on December 7, at 11 40 a m, pressure being recorded from the right femoral artery. At the beginning of the tracing, the pressure was 120 mm of mercury. The abdomen was opened at 11 50. The obstructed duodenal loop was raised and an intestinal clamp applied across the pylorus at 11 58. The blood pressure was 120 mm at 12 06 p m. At 12 15, a clot was removed from this vessel, and the cannula was transferred to the left femoral artery. The blood pressure was 128 mm of mercury. At 12 30, another clot formed, and the cannula was removed and placed in the right carotid artery. At 12 45, the blood pressure was 128 mm of mercury. Three milligrams of histamine mixed with a little of the intestinal contents from a normal loop was then injected into a mesenteric vein, this was followed by an immediate drop in pressure to 30 mm. A gradual rise then followed, which reached 90 mm of mercury at 1 15. A slow but gradual fall in pressure occurred during the next hour. At 2 10, the blood pressure was 60 mm of mercury. At 2 22, the arterial pressure had fallen to 40 mm. At this time, 50 mg of histamine was injected into a normal loop of the ileum, and intestinal clamps were applied across the bowel about a foot apart. A slow fall in pressure continued, death resulted at 2 35.

*Summary*—Duodenal obstruction was established and continued for twenty-one hours. The physiologic effect of histamine was noted after the injection of 3 mg of this drug into the mesenteric vein. Histamine was not placed in the obstructed duodenal segment. The pressure fell gradually from the beginning of the tracing. The injection of 50 mg into a normal ileal loop did not accelerate the drop.

EXPERIMENT 7 (dog 81) —Dec 20, 1926 Severed gut obstruction was established in the lower part of the ileum at 11 a m

On December 21, the dog was given 300 cc of a 3 per cent sodium chloride solution subcutaneously, when the tracing was made on December 22, the animal was in relatively good condition. Unfortunately, the tracing was lost, so measurements of the arterial pressure at any given time are not available. The following record of the experiment was written at the time the tracing was made. At 1 p m, when the tracing was started, the blood pressure was good. The abdomen was opened and the obstructed loop delivered. A rubber covered clamp was applied across the bowel about a foot proximal to the obstruction. One hundred milligrams of histamine was then injected with a fine hypodermic needle into the lumen of the bowel. Fall in pressure was not observed over an interval of one hour and fifteen minutes. At this time, a little of the intestinal contents

first, 50 mg and then of 25 mg more of histamine into the bowel was the same as it had been two hours previously when the experiment was begun. In another ileal obstruction of two days' duration, the dog was given 300 cc of a 3 per cent sodium chloride solution subcutaneously on the intervening day in order to improve his condition for the tracing, no fall in pressure was noted after one hour and fifteen minutes following the introduction of 100 mg of histamine into the obstructed bowel.

In five dogs, duodenal severed gut obstructions of two days' duration were established before the tracings were made. In three instances, 100 mg of histamine was placed in the obstructed loop at the time the blood pressure readings were made. In one instance, histamine was not introduced into the bowel. In another dog, 50 mg of histamine was placed in a normal loop in the ileum. In all five instances, a gradual reduction of blood pressure occurred. This effect was just as striking when histamine was not introduced into the obstructed loop. In two of the three instances in which histamine was placed in the obstructed segment, a great reduction of arterial pressure had occurred before the histamine had been injected into the obstructed bowel. Following the introduction of the histamine, no acceleration of this reduction was observed. It must be remembered that a dog with a duodenal obstruction of forty-eight hours' duration is not a good risk for a blood pressure tracing when the abdomen has been opened under either an anesthetic. These dogs usually survive the obstruction only about seventy-two hours. The gradual decline in pressure observed in these animals is probably thus best accounted for.

Histamine was slowly injected into a mesenteric vein of a normal dog and into a mesenteric vein of a dog with a duodenal severed gut obstruction of two days' duration. Histamine was introduced at the rate of 0.83 mg a minute. One hundred milligrams of histamine was dissolved in 100 cc of water, and the rate of the flow was so gaged that 100 mg would be injected every two hours (min 120). In both instances, a great and sustained fall of pressure occurred when the injection was begun. In another experiment in which the slow injection method also was practiced, but with interruptions, the same reduction in arterial pressure followed by a recovery on suspending the injection, was noted. When the instillation was resumed, the pressure fell, when discontinued again, a rise of the arterial pressure was observed. In all of the foregoing tracings made on normal dogs and those with severed gut obstruction, when histamine was introduced into the bowel, the consequence of increasing the pressure in the loop until it was tense by distending it with air and water was tested. No effect was observed. In another instance in which 100 mg of histamine was placed in a segment of bowel in a normal animal under a measured sustained pressure of 80 mm of mercury, reduction of the blood pressure had not occurred after an hour's observation.

from the ileum below the severed obstruction was aspirated and injected into the mesenteric vein without much effect. The same procedure was followed with a little of the contents of the loop proximal to the clamp which had been applied across the bowel. No great effect followed this injection. A few centimeters of the contents was then aspirated from the loop in which the histamine had been placed, and this was injected into a mesenteric vein and resulted in a great fall in pressure and in the death of the animal.

*Summary*—A severed gut obstruction was established low in the ileum and maintained for two days. The dog was given saline solution subcutaneously on the day following the obstruction, without a fall in pressure after one hour and fifteen minutes following the introduction of 100 mg of histamine into the loop of the obstructed bowel.

EXPERIMENT 8 (dog 90)—Jan 3, 1927. Duodenal obstruction was established in the dog at 3 p. m. A tracing was started on December 5, at 1 45 p. m. (fig 2). The arterial pressure was 120 mm. The abdomen was opened at 2 o'clock. The blood pressure was 104 mm. At 2 17, the loop was raised. The blood pressure was 98 mm. The duodenal loop was delivered and covered with warm packs of saline solution. A rubber covered clamp was then applied across the duodenum at the pylorus. In the meantime, the blood pressure had fallen to 60 mm of mercury. At 2 40, 100 mg of histamine was placed in the obstructed duodenal loop, the blood pressure had been falling gradually from the start. Acceleration was not noted, following this injection of histamine. At 3 08, the blood pressure was 60 mm. and at 3 23, 48 mm. At 3 30, 3 cc. of intestinal contents was aspirated from the obstructed loop and injected into a mesenteric vein with an immediate drop of pressure to 20 mm. At 3 40, the dog was dead.

*Summary*—A duodenal severed gut obstruction was maintained for two days. There was a gradual fall in pressure from the start. Acceleration did not occur following an injection of 100 mg of histamine into the obstructed loop.

EXPERIMENT 9 (dog 95)—Jan 6, 1927. Aseptic duodenal obstruction was established at 3 p. m. Two days later a tracing was started at 12 50 p. m. The blood pressure was 124 mm. The abdomen was opened at 1 o'clock, and the duodenal loop was delivered at 1 10. One hundred milligrams of histamine was injected into the obstructed bowel at 1 20. The blood pressure was 130 mm of mercury at 1 30. At 1 40, 108 mm., at 1 45, 90 mm., and at 2 10 it remained unchanged. A large portion of the contents of the obstructed loop into which histamine had been injected were then aspirated and injected into a mesenteric vein with an immediate drop in pressure to 50 mm of mercury. Death occurred at 2 15.

*Summary*—A severed gut duodenal obstruction was maintained for two days with a gradual decrease in pressure following an injection of 100 mg of histamine into the obstructed bowel.

EXPERIMENT 10 (dog 97)—Jan 10, 1927. Obstruction was established in the dog at 2 p. m. by severing the duodenum and turning in the ends of the bowel just below the pancreatic ducts. A tracing was started on January 12 at 11 50 a. m. (fig 3). The arterial pressure was 124 mm. The abdomen was opened at 11 55. At 12 o'clock, the arterial pressure was 106 mm. At 12 20, the arterial pressure was 110 mm of mercury. Histamine was not injected into the bowel in this experiment. The blood pressure was 100 mm at 12 46, at 12 55, 90 mm, at 1 10, 80 mm, at 1 30, 76 mm, and at 1 50, 60 mm. At

Tracings were made on eleven dogs in which strangulation obstructions were established by tightly constricting from 3 to 5 feet of the bowel and its mesentery with a gauze tie or by applying Carmalt forceps across the mesentery. In four instances, the strangulation was effected after the tracing was commenced. In the other animals, the strangulation was established aseptically at a period varying from two to six hours before the tracing was begun. Discoloration and thickening of the strangulated segment was noted in all instances. In a few dogs free fluid (hemorrhagic) was present in the peritoneal cavity. In two instances, histamine was injected into the strangulated bowel before the constricting mechanism was released. In the others, the effect on the blood pressure was noted when the ligature was loosened. In two animals with strangulation obstructions, the strangulated loop was irrigated until the contents returned clear at the initial operation. In another instance, the strangulated loop was irrigated until the contents returned clear at the time that the tracing was made, just before the constriction was released.

In every instance in which the strangulation had been established at some time previous to the recording of the blood pressure with a kymograph, a definite and great fall in pressure accompanied the release of the constriction, with a return of the normal luster to the bowel and pulsations in its vessels. This was obtained whether or not histamine had been placed in the bowel prior to the time the ligature was removed. Previous irrigations of the bowel did not obviate the reduction of the pressure when the strangulating mechanism was released. Subsequent injection of histamine into the damaged loop did not appear to accelerate the fall in pressure. When the ligature was reapplied about the strangulated bowel and mesentery, the reduction in pressure usually ceased, the pressure either maintained itself at the previous level, or, what seemed to be more common, exhibited a definite rise. Loosening of the ligature again after an interval of time almost invariably was followed by a decline of the arterial pressure.

In one of the four instances in which the strangulation was established at the time the tracing was made, a fall in pressure was not observed when the strangulation was released. A total anemia of a loop was created in this dog by clamping the mesentery with Carmalt forceps. In two other instances, repeated loosening and tightening of the ligature in these strangulations of shorter duration brought about a slow but gradual reduction of the blood pressure. In one of the animals (dog 15), however, a strangulation of only twenty minutes effected a material reduction in pressure. Fifteen minutes after the release of the constriction, a great reduction occurred. The pressure rose when the constriction was reapplied.

1 57, 10 mg of histamine was injected into a mesenteric vein, this was followed by irregular respirations and death occurred in three minutes

*Summary*—A severed gut duodenal obstruction was maintained for two days. There was a gradual fall in pressure from the time the abdomen was opened and the tracing started. Histamine was not placed into the bowel. Ten milligrams of histamine injected into the mesenteric vein killed this dog in two hours and two minutes after the abdomen was explored.

EXPERIMENT 11 (dog 142)—March 30, 1927. Histamine was slowly injected into the mesenteric vein of a normal dog by a dripping mechanism so that the rate of the flow could be accurately determined (fig 4). One hundred milligrams of histamine was placed in 100 cc of water. The rate of the flow was so gaged that 100 cc would run in in one hundred and twenty minutes (two hours). At the end of sixty minutes, 50 cc had been injected. The tracing of the pressure was started at 10 38 a m. A slow injection was begun at 11 05. Immediately there was a marked reduction in pressure. The pressure was sustained at this low level till death at 12 40 p m, when 76.85 mg of histamine had been injected at the rate of 0.83 mg per minute. At the beginning of the experiment, the pressure was 140 mm, after opening the abdomen, 120 mm, and when slow injection was started, 130 mm. A few seconds after injection was begun, the pressure fell to 30 mm. Occasionally it rose to 40 or 50 mm, but it continued at low level till death.

*Summary*—Eighty-three hundredths milligrams of histamine was injected into a mesenteric vein of a normal dog per minute. The pressure fell at once to a low level and was sustained by a continuous slow injection. Ninety-five minutes later, when 76.85 mg of histamine had been injected, death occurred.

EXPERIMENT 12 (dog 143)—April 1, 1927. A slow injection of histamine was made into a mesenteric vein of a dog in which intestinal obstruction had been established two days previously (duodenal obstruction). A tracing was started at 9 35 a m (fig 5). The abdomen was opened at 9 50. Slow injection was begun at 10 06. At 12 07 p m, 100 mg, had been injected. Death occurred at 12 17. At the beginning of the experiment the pressure was 140 mm. After opening the abdomen, the pressure was 135 mm, and at 10 06, when the injection of histamine was begun, 130 mm. There was a sudden drop to 80 mm about a minute after slow injection was started. In a few minutes, the pressure rose to 94 mm. One hour after slow injection had been started, the pressure fell to 65 mm. When 100 mg had been injected by this method at 12 07 p m, the pressure was 60 mm. Death occurred at 12 17.

*Summary*—Histamine was slowly injected into the mesenteric vein of a dog with a duodenal obstruction of two days. A gradual decline occurred after a sharp initial fall in the arterial pressure.

EXPERIMENT 13 (dog 144)—April 22, 1927. (1) Absorption of histamine from the normal bowel under a measured pressure of 80 mm, (2) interrupted slow injection of histamine into a mesenteric vein. A tracing was started at 10 55 a m at a pressure of 140 mm (fig 6). The abdomen was opened at 11 02 a m, the pressure was 130 mm. Following the opening of the abdomen, the pressure fell to 90 mm. At 11 10 a m, the pressure had risen to 100 mm, and rubber covered clamps were applied across the bowel to a segment of the upper part of the jejunum about 2 feet (60.9 cm) in length. One hundred milligrams of histamine was injected into the segment of the bowel, and a measured water pressure of 80 mg of mercury was established in the segment. The pressure rose to 110 mg of mercury at 11 20 a m. When the pressure was discontinued at 12 10

The subcutaneous administration of 50 mg of histamine brought about a gradual but definite fall in blood pressure in the one dog in which this procedure was carried out. Repetition of the injection occasioned a similar sustained fall of arterial pressure.

The injection into a mesenteric vein of peritoneal fluid from a dog in the peritoneal cavity of which a sterile loop of bowel removed from another dog had been allowed to autolyze, was accompanied by only a slight and transient fall in pressure. When the splenic pedicle was clamped off in another animal, release of the clamp almost five hours later was followed by only a slight and transient fall in the arterial pressure. A release of the constriction applied across the pedicle of the right kidney in the same dog, a few minutes later (more than five hours after the clamp had been placed on the renal vessels) was not attended by a change in pressure. In a dog in which both the aorta and vena cava had been clamped off two and one-half hours previously, change in pressure did not follow the removal of the clamps over a period of an hour. At the time the tracing was started, the dog was unable to stand because of the anemia in the hind quarters.

## COMMENT

In these experiments, no evidence was obtained that histamine was absorbed from the normal bowel or from the dog with a severed gut obstruction, at any rate, the physiologic reaction that accompanies intra-venous or subcutaneous administration of histamine, was not observed on the introduction of histamine into the bowel. If any absorption of histamine did occur from either the normal or the obstructed bowel, it was not absorbed as histamine. The immediate drop in pressure following the introduction of a few milligrams of histamine into a mesenteric vein demonstrates that the detoxifying influence of the liver is not great for histamine. If histamine was absorbed, it was detoxified in passing through the wall of the bowel. That the histamine did not disappear entirely from the bowel is demonstrated by the fact that aspiration of a few cubic centimeters of the contents of the bowel from the loop into which the histamine had been injected was always attended by a sharp fall in pressure that characterizes histamine action. This fall in pressure was always much greater than when intestinal contents alone were injected.

Hanke and Koessler<sup>6</sup> have been able to show by quantitative chemical tests for histamine that small quantities may be transported to the liver from the intestine in the normal animal. They have found that histamine is present as a normal constituent of the contents of the large intestine in both man and dog. They were able to isolate 53 mg of histamine in 150 mg of feces from a dog. From the liver of the same animal, 6 mg of histamine was obtained. They were unable to find

p m, one hour after the histamine had been injected, the pressure was 120 mm of mercury. Interrupted slow injection of histamine into the mesenteric vein was then begun two minutes later. At this time, after 8.33 mg of histamine had been injected, the systolic pressure fell to 60 mm. The slow injection was then discontinued, and in ten minutes the arterial pressure had risen to 100 mm. The slow injection was started again, and in ten minutes the pressure had fallen to 44 mm of mercury. The injection was again discontinued, and after ten minutes the pressure was 100 mm.

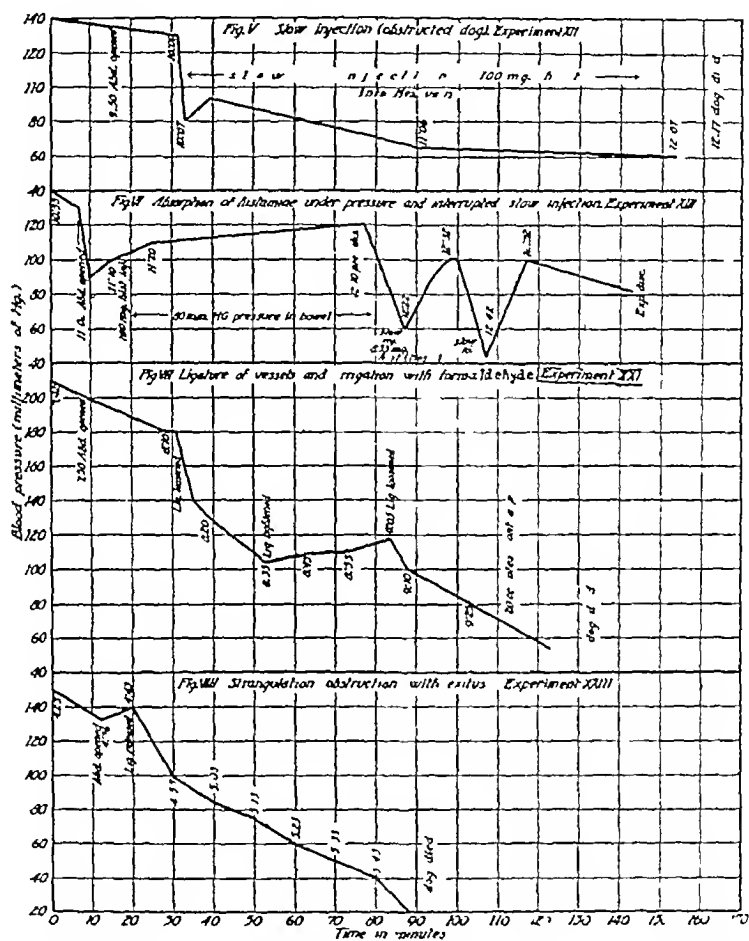


Chart 2—Figure 5, experiment 12 is a blood pressure tracing showing the effect of the slow intravenous injection of histamine in an obstructed dog, figure 6, experiment 13, blood pressure tracing showing the effects of the absorption of histamine placed in the bowel under pressure, and subsequent, slow, interrupted injection of histamine in the mesenteric vein, figure 7, experiment 21, blood pressure tracing showing the effect of ligation of vessels followed by irrigation of the bowels with formaldehyde, and figure 8, experiment 23, blood pressure tracing showing the effect of releasing the ligature which caused the strangulated obstruction.

**Summary**—1 One hour after 100 mg of histamine had been placed in a segment of the normal bowel under a sustained pressure of 80 mm of mercury, there was no fall in pressure. 2 On interruption of the slow injection of histamine into the mesenteric vein, the blood pressure recovered and fell again when the injection was resumed.



histamine in the intestinal content, the intestinal tract itself and in the livers of two guinea-pigs. They fed 100 mg of histamine to a normal guinea-pig, no manifestation of illness was apparent in the animal. A few hours later, when the guinea-pig was killed, only 1.6 mg of histamine was found in the intestinal contents. The alimentary tract itself contained no histamine. In some way, 98.4 mg of histamine had disappeared without causing death or eliciting any great symptoms. In another animal in which the same procedure was carried out, +7 mg of histamine remained in the intestinal tract, +5 mg had been transported to the liver. According to the authors, if the histamine that was not accounted for had been injected into the portal blood stream, the amount that would have entered the blood per minute would have been more than the dose necessary to kill a guinea-pig after a single intravenous injection. Results of the same nature were obtained when 500 mg of histamine was administered orally to dogs.

Koessler and Hanke<sup>9</sup> also established comparisons between the minimum effective dose of histamine that would lower the blood pressure in the dog when injected into a systemic and into a mesenteric vein. They found the figure for a systemic vein to be 0.0027 mg per minute per kilogram of body weight, 0.006 mg was necessary to cause a decided reduction in the arterial pressure in a mesenteric vein. The increased capillary bed of the liver, Koessler and Hanke stated, is responsible for the increased amount of histamine necessary to effect a reduction in pressure on injection into a mesenteric vein. Dale and Laidlaw,<sup>10</sup> Alekians and Harrington,<sup>11</sup> and Oehme<sup>12</sup> have made observations of the same nature with reference to intravenous injections of histamine into the portal and systemic circulations. This experiment demonstrates that the liver does not have a greatly detoxifying influence for histamine. Koessler and Hanke,<sup>9</sup> therefore, concluded that histamine is rendered pharmacologically inert in passing through the intestinal wall. Just what the fate is of the histamine placed in the normal bowel or the bowel with severed gut obstruction is difficult to state. Some of it probably is absorbed but is detoxified in passing through the wall of the bowel. Koessler and Hanke's<sup>9</sup> failure to find histamine present in any quantity in the intestinal tract or its contents would indicate either that it

9 Koessler, K. K., and Hanke, M. T. Studies on Proteogenous Amines, The Intestinal Absorption and Detoxication of Histamine in the Mammalian Organism, *J Biol Chem* 59: 889, 1924.  
 10 Dale, H. H., and Laidlaw, P. P. The Physiological Action of  $\beta$  Iminoazoly-ethylhistamine, *J Physiol* 41: 318, 1910-1911.  
 11 Alekians, J., and Harrington, C. R. The Relation of Histamine to Intestinal Intoxication. II. The Absorption of Histamine from the Intestine, *J Pharmacol & Exper Therap* 20: 45, 1922.  
 12 Oehme. Ueber die Wirkungsweise des Histamins, *Arch f exper Path u Pharmac* 72: 76, 1913.

EXPERIMENT 14 (dog 84)—Dec 23, 1926 Aseptic strangulated gut obstruction was established at 11 30 a m by tying a gauze ligature around 4 feet of the ileum and mesentery just snugly enough so that pulsations in the vessels beyond the ligature were not arrested. The dog was allowed to recover from the anesthesia. A tracing was started at 1 55 p m. The arterial pressure was 80 mm of mercury. The abdomen was opened at 2 01 p m at which time the blood pressure was 60 mm. At 2 13 p m it was 60 mm of mercury. Seventy-five milligrams of histamine was injected into the strangulated loop which was already discolored. The blood pressure had dropped to 40 mm of mercury at 2 30 p m. At 2 36, the constriction about the intestine and mesentery was released, and the pressure gradually declined to 30 mm of mercury. At 3 32 p m a few cubic centimeters of the intestinal contents were aspirated from the strangulated loop and injected into a mesenteric vein. Death resulted at 3 40 p m.

*Summary*—Venous strangulation obstruction was established for two and one-half hours. The blood pressure was low at the start, with a gradual decline. Seventy-five milligrams of histamine was placed in the strangulated loop. In thirty-five minutes after the abdomen was opened, the pressure had fallen from 80 to 40 mm of mercury. Constriction about the bowel and the mesentery was then released, with an accelerated fall in pressure.

EXPERIMENT 15 (dog 85)—Dec 27, 1926 Strangulation of the loop was established at the time of operation. A tracing was started at 11 10. The arterial pressure was 170 mm of mercury. The abdomen was opened at 11 17. A loop of the ileum about 4 feet in length was delivered at 11 22. A ligature was tightly placed about the bowel at 11 28, the pressure at this time being 160 mm. At 11 48 the pressure was still the same. The ligature was loosened a little with a just perceptible fall in pressure. At 12 o'clock, the ligature was loosened a little further, with a more definite fall in pressure in two or three minutes. At 12 07 p m, the pressure had dropped to 110 mm of mercury and the ligature was removed with a rather sharp decline in pressure. At 12 14 the pressure had fallen to 80 mm, and the ligature was again tightened. At 12 30, the pressure had risen to 130 mm. At 12 34, the ligature was again loosened, and at 12 45, the pressure had fallen to 118 mm. The ligature on the bowel was alternately tightened and loosened three more times with less reaction following each release of the constriction, but with a gradual decline of the arterial pressure. During the time that the constriction was maintained, the blood pressure was definitely sustained with little rise in pressure, but with each release a gradual fall occurred. The blood pressure at 1 30 p m was 90 mm. At 1 45, 50 mg of histamine was injected into the bowel without an additional fall. At 2 20, the pressure was 64 mm. A few cubic centimeters was aspirated from the strangulated loop into which the histamine had been injected. Death occurred at 2 30 p m.

*Summary*—Strangulation obstruction was established at the time the tracing was made. Twenty minutes later, the constriction was released, accompanied by a fall in pressure. When the ligature was tightened, the pressure rose. Two hours later, histamine was placed in the strangulated loop without an additional fall being noted.

EXPERIMENT 16 (dog 86)—Dec 28, 1927 Strangulation obstruction was established. A tracing was started at 10 50 a m. The blood pressure was 170 mm. The abdomen was opened at 10 57 without any change in the blood pressure. At 11 20, a loop of the ileum 3 feet in length was strangulated, together with its

was almost completely absorbed and rendered innocuous in passing through the intestinal wall, or that it was destroyed within the lumen of the bowel. After histamine had been placed in a normal loop or segment of the bowel that had been obstructed previously, and a few cubic centimeters of the contents from such a loop had been aspirated and injected into a mesenteric vein, we were always able to elicit a decided histamine action after the lapse of an extended interval of time. The reduction in pressure accompanying such an injection was always greater and sustained for a longer time than the occasional reduction following the injection of intestinal contents from other segments in which histamine had not previously been placed. Gerard<sup>5</sup> stated that he was able to isolate 14 mg of histamine from a closed colon loop in a dog eight months after Dragstedt had established the obstruction. In this animal either this amount of histamine remained in the bowel and resisted absorption as well as destruction in the lumen of the bowel, or it had its origin in the intestinal secretion formed by the mucosa of the obstructed segment. Koessler and Hanke<sup>6</sup> granted that their quantitative method for histamine determination in fecal content is only about 60 per cent effective.

Stone and Frior<sup>12</sup> intimated that in occlusion of the bowel, the distention per se, by increasing the intestinal pressure, is a big factor in absorption from the obstructed bowel. When histamine was placed in a segment of the intestine under a measured sustained pressure of 80 mg of mercury, we were unable to detect any evidence of absorption of the histamine.

Meakins and Harington<sup>11</sup> placed histamine (histamine-phosphate) in various segments of the normal intestine in cats. They found that a rather sharp fall of pressure occurred a few seconds after the introduction was made. They stated this fall was more noticeable in the ileum, slightly less so in the duodenum and much less after the introduction of histamine into the stomach or cecum. When the blood pressure was gradually falling, they were unable to accelerate the fall by the introduction of more histamine. They believed that a sudden primary fall in pressure accompanying the introduction of histamine into the bowel should be the rule, and that failure to observe it may be due to the presence of semidigested food in the intestines.

We were never able to confirm this observation in the dog. Failure to depress the blood pressure even more on the introduction of a greater quantity of histamine into the bowel would indicate that no great amount of histamine as such was absorbed and would lend tenuous support to

<sup>13</sup> Stone, H. B., and Frior, W. M. Absorption in Intestinal Obstruction, Intra-Intestinal Pressure as a Factor, *Proc South Surg A Abstr J A M A* 84:141 (Jan 10) 1925.

mesentery, by being constricted tightly with a gauze tie. At 11 42, the ligature was loosened without causing a definite change in the arterial pressure. At 11 55, the loop was again constricted and loosened at 12 20 p m with a gradual but definite fall of pressure to 140 mm. At 12 42, the ligature was tightened again and loosened at 1 16, following this, there was a slight and gradual fall of pressure to 120 mm. When the loop was constricted again at 1 30, the pressure continued to fall slowly. At 1 45, the pressure was 100 mm. The loop was untied at 1 50 without much effect. At 2 05 p m, 10 mg of histamine was injected with an immediate depression of pressure to 40 mm of mercury, death followed.

*Summary*—Strangulation obstruction was established at operation. Twenty-two minutes later, the constriction was released without a fall in pressure. The ligature was tightened again and loosened after twenty-five minutes, with a definite fall in pressure. An injection of only 10 mg of histamine into a mesenteric vein killed this dog after the ligature had been alternately tightened and loosened over a period of two hours and forty-five minutes.

EXPERIMENT 17 (dog 87)—Dec 28, 1926. Strangulation obstruction was established. A tracing was started at 2 35 p m, the arterial pressure being 180 mm of mercury. The abdomen was opened at 2 40. At 2 55, the blood pressure was 144 mm. At 3 00, the loop of the ileum and its mesentery, about 3 feet in length, were ligated with a gauze tie. At 3 25, the arterial pressure was 164 mm. At 3 30, the constriction about the bowel and the mesentery was released without causing any change. The blood pressure was 160 mm of mercury. At 3 40 another loop of the ileum near the cecum, also about 3 feet in length, and its mesentery, were constricted with a gauze tie. The ligature was released at 4 o'clock, and a slow fall in pressure to 120 mm occurred. At 4 35 the loop was again constricted. The blood pressure was 130 mm of mercury at 4 55. At 5, the ligature was loosened, this was followed by a slow fall of pressure to 118 mm. At 5 05, 5 cc of intestinal contents was aspirated from this loop and injected into a mesenteric vein, causing a fall in blood pressure to 78 mm. At 5 15, another such injection was made. The dog died at 5 30.

*Summary*—Repeated constriction and release of strangulation was accompanied by a slow but gradual fall of arterial pressure.

EXPERIMENT 18 (dog 88)—Dec 29, 1926. Strangulated obstruction of about 5 feet (152 cm) of midileum was established at 11 40 a m by placing a tight gauze tie about the bowel and the mesentery under aseptic technic. The dog was allowed to recover from the anesthesia. A tracing was started at 1 45 p m under ether anesthesia. The blood pressure was 176 mm of mercury. The abdomen was opened at 1 50 and a slight but sharp fall in pressure followed. At 1 55 the pressure was 144 mm, at 2 it had risen to 160 mm. At 2 05, the strangulated loop was delivered with a sharp fall to 124 mm of mercury. At 2 10, the blood pressure had risen to 150 mm. The bowel was a blackish-blue and indurated to touch. The ligature constricting the bowel and the mesentery was loosened with an almost immediate fall in blood pressure to 110 mm of mercury. At 2 20, the ether anesthesia was light, a short convulsive seizure occurred, during which the blood pressure rose to 130 mm of mercury, this was followed by a sharp decline to 84 mm of mercury, above which the pressure never rose again. At 2 35, the arterial pressure was 80 mm and at 2 40, the systolic pressure was 40 mm. At 2 47, the blood pressure was 56 mm, at 3 and at 3 09, 62 mm. The ligature was again tightened about the loop, this was followed by a slight but transient rise in pressure at 3 15 to 76 mm.

the belief that the primary fall in pressure was not occasioned by histamine alone. Unless the blood pressure fell to such an extent that the animal was in a state of shock, the introduction of more histamine into the bowel, if absorbed as such, should depress the blood pressure as did the first injection.

It is generally known that ether anesthesia makes an animal much more susceptible<sup>14</sup> to the effects of histamine. It is stated that an unanesthetized dog can tolerate ten times the amount<sup>15</sup> that an animal under the influence of ether can. Most of our experiments on histamine absorption were made on etherized animals. Failure to elicit the histamine effect by placing it in the lumen of the bowel of these dogs with simple gut obstruction would indicate that no great amount of histamine was absorbed.

The marked fall in blood pressure that accompanies the release of the constricting mechanism in strangulation obstruction demonstrates that autolysis of the intestine deprived of its blood supply progresses rapidly and is accompanied by a rapid liberation of toxic material that gives a histamine-like effect. An effect of this nature was not observed when the kidney or splenic pedicle was clamped off for five hours. It was not seen after ligation of the aorta and vena cava for three hours. The accumulation of carbon dioxide behind the strangulation therefore was not the cause of the fall in pressure when the ligature was released. This fall in pressure seemed greater when there was venous stasis than in the presence of total anemia. This observation is in harmony with the statement of Bayliss<sup>16</sup> that the metabolism in the tissue is increased in the presence of venous stasis. Irrigation of the bowel at the time that the strangulation was established or just before the release of the obstructing mechanism did not prevent the fall in pressure when the ligature was removed. Tightening the ligature again usually brought about a rise of pressure, denoting that the absorption was disturbed. Replacing the removed intestinal contents in the bowel or injecting histamine into the lumen of the strangulated segment did not seem to accelerate the fall.

The only type of tissue in the wall of the bowel that differs materially from that of muscle, kidney or spleen is the mucosa. Depriving the intestine of blood probably occasions an autolysis of the mucosa of the bowel and therefore liberation of a toxic substance. It would seem

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14 Cannon, W. B. Traumatic Shock, New York: D. Appleton & Co. 1923, p. 163. Dale, H. H. Report of Shock Committee, Medical Research Committee No. 26, March 14 1919, p. 15.  
15 MacLeod, J. F. R. Physiology and Biochemistry in Modern Medicine, St. Louis, C. V. Mosby Company, 1922, p. 308.  
16 Bayliss, W. M. Principles of General Physiology, New York, Longmans & Company, 1924, p. 422.

Fig 27—Photomicrograph made from the paraffin block shown in figure 25. This is approximately the actual size of the tumor removed at operation. It will be noted that at the top of the section can be seen several lobules of hyperplastic parenchyma which by pressure on the adjacent normal thyroid parenchyma have formed apparent capsules. The lower two thirds of the section is occupied by a large mass of tumor nodule which stains homogeneously pink with eosin and is composed mainly of white fibrous connective tissue cellular detritus and some material that looks like colloid. However, no active thyroid tissue can be seen. Reduced from an enlargement to twice the normal size.





Fig 28 —Higher magnification of figure 27 to show and compare the constituents of the large tumor mass, the small nodule of hyperplastic tissue and the compressed normal thyroid parenchyma. It is obvious that the main tumor mass in this specimen was without function, as there is nothing but inert material constituting this tumor and that the active portion of the gland and that region responsible for the hyperactivity of the thyroid is located in the upper portion or in the region showing the hypertrophy and hyperplasia. The sharp localization of this hyperactive tissue in the otherwise normal parenchyma is striking. The main tumor mass does not suggest a neoplasm, but on the other hand atrophic degenerated parenchyma resulting from previous hyperinvolution and probably involution of a once hyperactive parenchyma. It is, of course, plain that enucleation of this inert mass would not have cured the patient and that this tumor per se probably played no role in the production of the clinical syndrome but was a coal of a fire that has burned, or an area of extreme hyperinvolution. Reduced from an enlargement to four times the normal size.

that a damaged mucosa would be more permeable than the normal one to absorption from the lumen of the bowel. In these experiments, however, it would appear that autolysis of the wall of the bowel rather than an increased absorption from the lumen occasioned the depression of blood pressure.

Meakins and Harington<sup>11</sup> damaged the mucous membrane of the intestine by tying off the arterial supply of the part under investigation and then injected histamine. When the blood supply was arrested in this manner for from five to fifteen minutes and histamine was placed in the bowel, a marked primary fall was observed, but there was not a tendency toward a gradual and continued decline. This occurrence, the authors felt, indicated that the absorption of histamine took place rapidly and then almost ceased. Our observations would indicate that it was injury to the mucosa itself rather than absorption from the lumen that brought about the fall in pressure. We do not, of course, deny that absorption is not increased over that from the normal bowel or the segmentally obstructed bowel. As previously indicated this was our assumption, but the fall in pressure in the irrigated strangulated loop and the failure of the injected histamine to accelerate the drop in pressure would not support such a contention.

In the strangulations of short duration, only transient and slight reductions in blood pressure were observed when the constriction was released. In some instances, a fall in the pressure was not obtained. In the strangulations established a few hours previously, the fall in pressure was constant when the strangulation was released. In one animal (experiment 23, fig 8), the blood pressure gradually declined, and the dog died as a result of this alone, although the pressure had been good before the constriction was released. In a few animals with strangulation obstruction, the pressure was low when the tracings were begun. In these animals it would appear that the visceral peritoneum of the strangulated intestine had become permeable to the toxic substance liberated by the damaged mucous membrane, and that absorption was occurring through the peritoneal cavity. For how otherwise could absorption occur with the lymphatics and mesenteric vessels obstructed?

It would also appear that when the blood supply to a segment of the bowel is disturbed by increasing the tension within the lumen a similar fall in pressure should be noted. Van Zwahlenburg<sup>17</sup> has examined vessels of the intestinal wall with a cystoscope in the lumen of the bowel and has found that states of venous and arterial anemia may be produced by increasing the distention in the loop. The distention ulcer, however, observed so frequently on the antimesenteric border of the

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<sup>17</sup> Van Zwahlenburg, C. Strangulation Resulting from Distention of Hollow Viscera, *Ann Surg* 46:780 1907.



dose of thyroid extract was increased, a return to the normal rate and a more stable metabolism was noted. This was accompanied by an amelioration of the symptoms.

*Juvenile Rheumatism*—From a statistical study of the incidence of rheumatic fever in children in London, Benjamin<sup>24</sup> concluded that it is a disease of poor people and that the incidence of the disease is in direct relation to the degree of the poverty.

Miller<sup>25</sup> made a comparison between the reports of the British Medical Association and those of the Medical Research Council on arthritis, and drew the following conclusions in regard to the importance of six supposed etiologic factors. 1 Influence of social status. They agreed that it is a disease of the poor, but not necessarily of the poorest. 2 The influence of heredity. It was agreed that heredity is of no influence. 3 The influence of school environment. The home rather than the school is the causative factor, as those children who were taken from homes in the "rheumatic stratum" and placed in special schools escaped. 4 The influence of tonsillar disease and tonsillectomy. Diseased throats were found in from 75 to 83 per cent of the patients. The removal of the tonsils does not prevent chorea. 5 The influence of contagion. Contagion is, at most, of the slightest importance. 6 The influence of damp dwellings. "There is nothing in the theory of damp houses as a causative factor."

*Incidence of Hypertrophic Arthritis*—Garvin<sup>26</sup> made an investigation of the incidence of hypertrophic arthritis of the spine in a series of 2,090 patients more than 50 years of age, who, without complaint of symptoms in the back but because of suspected urinary disorders, were subjected to roentgenologic examination of the kidneys, bladder and ureters during 1925. What Garvin designated as "incidental hypertrophic arthritis of the spine" was found in 40 per cent of the women and in 67 per cent of the men. Garvin discussed the possible etiologic factors, such as abscessed teeth, infected tonsils, etc., the presence of a traumatic factor, such as obesity, in which the assumption of chronic trauma can be made and also the evidences of senescence. He stated that in view of the high incidence in persons beyond 50 years of age, especially in men, of hypertrophic arthritis of the spine, unaccompanied by any symptoms in the majority of the patients, the condition should be considered and treated conservatively. He pointed out the obvious improbability of any single accident or injury being responsible for the development of hypertrophic arthritis.

*Hypertrophic Arthritis of the Cervical Spine*—Forrester<sup>27</sup> described various thickenings noted on the transverse processes of the cervical

24 Benjamin, F. J. Lancet 1-1175 (June 4) 1927  
 25 Miller, Reginald. Brit. M. J. 1 932 (May 28) 1927  
 26 Garvin, J. D. Hypertrophic Arthritis of Spine, Arch. Surg. 15 118 (July) 1927  
 27 Forrester, Henry. Lancet 2 65 (July 9) 1927

dog with an obstructed intestinal loop (both ends turned in) and in the patient with strangulation obstruction, is rarely seen in the patient with simple intestinal obstruction. We have never seen it in a large number of dogs in which simple obstruction of the gut has been established. The damage to the wall of the bowel in simple obstruction in which the intralumen tension is increased rarely approximates that observed in strangulation obstruction.

#### CONCLUSIONS

1 Absorption of histamine from the normal small intestine (duodenal and ileum, of the dog and in simple obstruction of the small intestine of two days' standing cannot be detected by the physiologic test for histamine.

2 In strangulation obstruction, a great fall in arterial blood pressure occurs following the release of the strangulating mechanism.

3 The autolysis of intestinal mucosa deprived of its blood supply is rapid and is accompanied by the liberation of a toxic substance that gives an effect like that of histamine.

4 The absorption of histamine from the lumen of a strangulated segment that is still viable does not appear to be great.

vertebrae in patients suffering from chronic arthritis. He expressed the opinion that these thickenings frequently give rise to occipital headaches and neuralgic pains radiating down the arms. That osteo-arthritis of the cervical spine may cause serious pressure on the nerve roots, was pointed out by Hendry and Fowler.<sup>28</sup> They examined a patient who showed marked muscular weakness and sensory disturbance of one arm, without pain, in whom the symptoms were ascribable only to this cause.

#### TUBERCULOSIS

*Remote Results of Operative and Nonoperative Treatment for Tuberculosis of the Ankle in Children*—Pouzet<sup>29</sup> made an investigation of the results of treatment, both nonoperative and operative, in children with tuberculosis of the tibiotarsal articulation in Nové-Josserrand's clinic at Lyon. The statistics cover a group of 104 patients, all children under the age of 16, who were treated between 1898 and 1922, inclusive. The minimum period of observation was three years. The study was limited to those cases in which the primary focus of disease had been in the tibio-astagalar articulation, with or without secondary invasion of other bones or joints, and did not include those with diffuse lesions starting simultaneously in all the tarsal bones. It has been the general policy in the clinic to employ immobilization as the best method of treatment, except in rare cases in which the severity of the process or the presence of a complication made surgical intervention necessary. The parts were encased in plaster, and the castings changed at intervals of three months. Open air, sunlight, and other antituberculous measures were also employed. When the tuberculous process appeared to extend, or when progress seemed to be uncertain, surgical intervention was resorted to. The results were graded as normal—meaning absence of functional impairment, very good—excellent function, but with minor troubles, such as limp when tired, good—slight limp, with walking capacity exceeding 10 kilometers, fairly good—limp, with walking capacity of from 5 to 10 kilometers, and bad.

The results in general in a total of 104 patients, of whom ninety-one were treated by immobilization, were as follows: Cure was obtained in sixty cases, or 66 per cent, in eighteen the feet were normal, in twenty-eight the results were very good, and in fourteen the results were good or fairly good. (Four of these patients died later, after the local lesions had healed.) Failure resulted in thirty-one cases, or 34 per cent. Four patients died during treatment, twenty-seven required operative intervention, twenty because of extension and seven because of recurrence.

<sup>28</sup> Hendry, A W, and Fowler, Andrew. *Lancet* 1 1181 (June 4) 1927.  
<sup>29</sup> Pouzet, F. *Rev d'orthop* 14 99, 1927.

# THIRTY-FIFTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY\*

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## CONGENITAL DEFORMITIES

*Congenital Dislocation of Knee*—Spiers<sup>1</sup> reported four cases of congenital luxation of the knee. Of these, three were cases of double luxation and one of single luxation. In all cases the tibia and fibula were displaced forward, upward, and laterally. Only the patient with the single dislocation was treated by the author. Manipulative reduction was performed under an anesthetic and the deformity corrected, the knee being immobilized in plaster in a position of from 35 to 40 degrees flexion. Satisfactory progress was reported at the end of six weeks, when the patient was last observed.

*Congenital Torticollis*—From a study of thirty-seven patients with wry neck observed at Spitzzy's Clinic in Vienna during the last two years, Aberle<sup>2</sup> has drawn the following conclusions. Congenital wry neck is to be considered as "vitium primae formationis." It is found in association with other congenital deformities and may be present in several members of the same family. The patients may be classified in three groups: (1) patients with oblique posture of the head and asymmetry but without discoverable changes in the sternomastoid muscle, (2) patients with marked changes in one of the sternomastoid muscles, but without evidence that the muscle was injured at birth, and (3) patients with injury of one of the sternomastoid muscles superimposed on a prenatal degeneration of the muscle. The author agrees that an

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\* This Report of Progress is based on a review of 196 articles selected from 429 titles dealing with orthopedic surgery appearing in medical literature between July 2, 1927, and Sept 24, 1927. Only those papers which seem to represent progress have been selected for note and comment.

1 Spiers H W. J Bone & Joint Surg 9 469 (July) 1927

2 Aberle W. Ztschr f orthop Chir 49 27 1927

Just as good results were obtained in the cases in which sinuses were present as in those in which they were not. The younger the patients the better were the results. The severity of the disease seemed to increase with age, and the older the patients the higher the number of deaths and the greater the necessity for resorting to operative treatment. The cures were fairly permanent, with recurrence in only 3.5 per cent of the patients. The author does not consider ankylosis the best result, but, on the contrary, stated that a certain degree of mobility helps in walking, without apparently increasing the risk of recurrence. Roentgen-ray examination showed a perfectly normal foot in a few cases, in others, lesions limited to the articular surfaces, such as irregularity of the joint space, exostoses and osteophytes, fibrous and bony ankylosis, and flattening of the astragalus. Hypermobility developed in the uninvolved joints to compensate for stiffness in the diseased joints. The diseased foot showed retardation of growth, and was always shorter than the normal one. In a few cases there was a shortening of the tibia of from 1 to 3 cm. No deformities of the foot were noted except pes cavus in three instances.

The patients in whom conservative treatment failed (thirty-nine of 104) and operative measures had to be employed also were studied. The cases were classified as follows: twenty-five late interventions after immobilization was tried, eighteen because of aggravation, and seven because of early recurrence, fourteen early interventions necessitated by the extent and severity of the process. The operations consisted in astragalectomy and localized tarsectomy. In the beginning, the proportion of astragalectomies was high, but as the efficacy of more conservative procedures was demonstrated, the number of astragalectomies decreased. Bony lesions were noted in the astragalus thirty-nine times, in the tibia twenty, in the calcaneum twenty-five, in the scaphoid two, and in the cuboid five. The average period required for a cure with complete healing of sinuses and the possibility of walking was about eleven months after astragalectomy and thirteen months after tarsectomy. Of the thirty-nine patients, cures were obtained in twenty-eight, or 73 per cent, on one amputation was performed, and one is still under treatment. There were nine deaths, or 23 per cent. The fatalities occurred chiefly in young patients and were due to the severity of the process rather than the result of the interventions. From a study of the results the author concluded that operative treatment is capable of preserving a useful foot in a large number of patients with tuberculosis of the posterior tarsus. Although the results of the two methods cannot be compared because of the difference between the disease processes in the two groups, Pouzet stated his belief that treatment by immobilization should be tried in children, and that only after a thorough trial without improvement, or in the case of a severe lesion, should surgical interven-

injury to a normal sternomastoid muscle may be followed by the formation of an hematoma, but expressed the opinion that this heals in a short time and is not necessarily followed by wry neck. The asymmetry of the head and face associated with congenital wry neck is not hemiatrophy but the general reaction of the bone to pressure, with resulting hindrance of growth. The asymmetrical development tends to increase but may be arrested by early operative correction of the deformity.

[ED NOTE—Aberle's theory that injury of the sternomastoid muscle, sustained at birth, is not sufficient to account for congenital torticollis is interesting, but the evidence he has adduced is insufficient to prove his contention.]

*Congenital Radio-Ulnar Synostosis*—Pepi<sup>3</sup> wrote on the subject of congenital radio-ulnar synostosis at the upper ends of the radius and ulna, and expressed the belief that the best method of restoring pronation and supination is the operation described by Galeazzi. This consists of a transverse osteotomy of the radius at a level a little above the insertion of the pronator radii teres, with the removal of a section of the bone, and the production of a pseudarthrosis at this point.

[ED NOTE—Authors who have made a study of congenital radio-ulnar synostosis have stated that excision of the head and neck of the radius usually fails to restore the rotary movements of the forearm. The synostosis usually recurs. Galeazzi's operation has advantages in this respect, as it is performed at a distance from the synostosis.]

#### ENDOCRINE DISORDERS AND THERAPY

*Acromegaly*—In the annual oration delivered before the London Medical Society, Cushing<sup>4</sup> summarized the present knowledge of the function of the hypophysis. H. M. Evans is credited with the discovery that anterior lobe extracts would stimulate growth. It is difficult to obtain an active extract, and great variation is found in the commercial products. Experiments with the extracts have not produced acromegaly, but gigantism. Gigantism is probably the result of a process which has started before the epiphyses have become ossified, whereas acromegaly is an expression of the same influence acting after epiphysial growth has ceased. Cushing classified the pituitary syndromes as follows:

*A. Hypopituitarism*. Absolute privation of hypophysis probably leads through cachexia to death.

*B. Hypopituitarism*. 1. Anterior lobe deficiency due to ischemic necrosis (Simmond's disease). Simmonds reported thirteen cases of destruction, partial or complete, of the anterior lobe, many by septic infarcts. The counterpart of dwarfed animals thus exists in the dwarfed persons and results from disturbance of hypophysis in early life.

3 Pepi, C. *Policlinico* 34:205 (May 15) 1927.

4 Cushing, Harvey. *Brit. M. J.* 2:1 (July 2) 1927.

[Ed. Note—We wish to call attention to the fact that when patients with supposed tuberculosis of the joints are treated nonoperatively, it is always difficult to be certain of the diagnosis.]

#### POLIOMYELITIS

In a recent editorial in the *Journal of the American Medical Association*,<sup>30</sup> the knowledge of infantile paralysis has been well summarized. Cases of poliomyelitis have been divided into three classes: (1) those with characteristic paralysis, (2) those without paralysis, but exhibiting symptoms indicative of meningeal irritation and usually minor disturbances of the motor centers, the so-called abortive type, and (3) those showing symptoms similar to the initial symptoms of known cases of infantile paralysis, but without definite indications of involvement of the central nervous system. In discussing the treatment it has been stated that there is every reason to believe that rough handling of the spine and manipulation, as practiced by chiropractors and members of other cults, renders impossible the recovery which might otherwise take place in some of the affected nerves. The author considers that the only effective method of prevention is complete isolation from contact with patients in all stages of the disease, including convalescents and carriers. It has been recommended that during an epidemic until cold weather sets in children should not travel about any more than is absolutely necessary. No specific prophylactic treatment that can be applied practically has yet been discovered.

We have noted a recent report by the Council on Pharmacy and Chemistry of the American Medical Association<sup>31</sup> of its refusal to accept for inclusion in New and Nonofficial Remedies poliomyelitis antistreptococcus serum. This action was based on the following objections: 1. The organism from which the serum is produced is not generally accepted as the etiologic agent of poliomyelitis. 2. The published reports on the serum are generally favorable, but there is considerable question as to whether the groups of control cases are directly comparable. 3. It has been found that on account of widespread favorable newspaper publicity given the serum, the physician often feels compelled to use it, though he is not convinced of its efficacy. Indeed, laymen often demand its employment. In our estimation, the Council has taken the proper stand in refusing to accept any poliomyelitis antistreptococcus serum until more positive evidence for its usefulness becomes available.

#### PYOGENIC INFECTIONS

*Osteomyelitis*—In discussing infections of the bones and joints in children, Stone<sup>32</sup> pointed out that while epiphyseal separation is a ill

30 Infantile Paralysis, Editorial, J. A. M. A. 89 1662 (Sept. 24), 1927.  
 31 Poliomyelitis Antistreptococcus Serum Reports of Council on Pharmacy and Chemistry, J. A. M. A. 90 617 (Feb. 25), 1928.  
 32 Stone, J. S. Boston M. & S. 1 197 367 (Sept. 29), 1927.

2 Deficiency syndromes due to compression of parhypophyseal tumors (Frohlich's disease) This syndrome is less cleancut than Summoud's disease, because of the different parts of the gland and of the adjacent structures that may be involved, particularly the hypothalamus. The patients are mentally alert, but show extreme degrees of adiposity or emaciation, polyuria or the reverse, dwarfism, sexual infantilism, or premature physical senility. Cushing has encountered in all, eighty-one verified examples of these parhypophyseal tumors. 3 Hypopituitary states associated with chromophobe adenomas. Of all pituitary syndromes these are most often encountered. Cushing had 188 in his series. They occur almost exclusively in adult life. The disorder is common, as common, in all probability, as goiter. One cannot diagnose this condition without definite local evidences of the growth. Changes almost always occur in adult life and are limited to the tendency to adiposity, loss of hair, sexual dystrophy, etc. It is not unusual for this condition to be treated as myxedema. Ordinarily the sella is greatly distended.

C Dyspituitarism. This is a mixed group of syndromes in which hyperpituitary symptoms have been superseded by the reverse state.

D Hyperpituitarism. 1 Gigantism—Gigantism is due to chromophile adenomas originating in preadolescence. Cushing has seen sixty-five patients with such tumors. They are much oftener found in adults, hence acromegaly is much commoner. 2 Acromegaly—*acromegalia* adenomas of adult life. Acromegaly calls attention to itself before the adenoma has reached the tumefaction stage. Cushing feels justified, in view of the low mortality (41 per cent), in attacking the tumors early while the sella was still small. He noted as postoperative results (1) loss in weight, (2) lowered metabolic rate, and (3) relative intolerance to carbohydrates. By partial hypophysectomy the intolerance may be reduced and existent glycosuria checked. Complete extirpation is to be avoided lest diabetes insipidus, excessive adiposity, and even a fatal cachexia supervene. Only when substitution therapy has been made practical will this risk be overcome.

Davidoff and Cushing<sup>5</sup> stated their belief that acromegaly represents a state of hyperpituitarism of the acidophil cells of the pars anterior. They consider that there are ample reasons in support of the view that the meliturias which occur in 25 per cent of all cases of acromegaly are primarily hypophyseal, even though the pancreatic islets play a secondary rôle in their production.

In seven patients with acromegaly (four women and three men), Castex and Schteingart<sup>6</sup> found the basal metabolism increased in three

5 Davidoff, L. M., and Cushing, Harvey. Studies in Acromegaly, *Arch. Int. Med.* 39: 751 (June) 1927.

6 Castex, M. R., and Schteingart, M. *Rev. Soc. de med. int. y fisiol.* 3: 66, 1927.



recognized, the frequency with which an epiphysis may be loosened without actually being displaced is not generally appreciated. Similarly, subperiosteal and greenstick fractures are seen more often in children because of the relatively greater thickness of the periosteum. The importance of these and other mild injuries in relation to infection lies, according to the author, in the fact that areas of increased susceptibility to infection are produced in the regions of the epiphyses by the trauma Bocchini<sup>33</sup> also has been convinced from a study of the literature that trauma plays an important part in providing an area of lowered resistance in the bone to infection. Discussing acute osteomyelitis of the spine, he stated that the vertebral body is involved more commonly than the neural arch. If the body is involved the prognosis is grave, if the neural arch is involved it is less grave. Of the neural arch the author has found the lamina more often affected, but either the spinous process or the transverse process may be affected. When the involved area of the spine is accessible he has recommended surgical intervention.

*Control of Wound Infection*—Orr<sup>34</sup> pointed out the necessity of following three fundamental rules in the treatment of infected wounds (1) a thorough primary operation, aseptically performed, (2) the avoidance of secondary infection in the postoperative dressings, and (3) immobilization, in correct position, of all injured parts until healing has been established. He advocated packing the wounds with gauze on which petrolatum has been smeared, and fixation of the parts in plaster at the time of operation. By this method he considers it unnecessary to change the dressings more often than at intervals of from three to four weeks, and not infrequently the infected bone cavities heal completely with only one or two dressings.

[ED. NOTE—Approaching this method with grave doubts as to its safety and recognizing its possible dangers unless the patients are carefully watched, we have been able to confirm Orr's claims in a small group of cases. We agree that the thoroughness of the operation is of prime importance and that unnecessary postoperative dressings are to be avoided. Whatever other arguments may be advanced in support of this method, the humanitarian one of reducing painful dressings to a minimum, especially in children, is a powerful one.]

#### VASCULAR DISEASES

*Thrombo-angitis Obliterans*—Lian, Puech and Viau<sup>35</sup> made an investigation of fifty-two patients with endarteritis obliterans, with the purpose of shedding some light on the etiology of the disease. Dis-

33 Bocchini, A. *Pediatrics* 35:554 (May 15) 1927.  
 34 Orr, H. W. *Minnesota Med* 10:362 (June) 1927.  
 35 Lian, Puech and Viau. *Bull et mem Soc med d hôp de Paris* 51:534 (May 5) 1927.

and normal in four. The largest increase was 31 per cent. They concluded from their studies that simple acromegaly without change in the tubers or in the posterior lobe of the pituitary causes an increase in metabolism. The complicated type of acromegaly does not produce this effect.

*Parathyroid Hormone and Calcification of Fracture Callus*—Lehman and Cole<sup>7</sup> conducted some experiments on animals to determine the effect of injections of parathyroid extract on the calcification of fracture callus. *A priori* they did not believe that the extract would hasten or aid in inducing the deposit of callus, because its action is to mobilize the fixed calcium in the body, and as Hunter and Aub have shown, the excess of calcium in the blood serum of patients who have had parathyroid extract comes largely from the bones. The results of the experiments show that parathyroid extract does not hasten the calcification of fracture callus. The only effect noted in rats is a tendency to delay the process.

On the other hand, Hueper<sup>8</sup> performed some experiments which led him to draw the opposite conclusion. He stated that repeated injections of parathyroid extract apparently stimulate the production and calcification of osteal tissue. However, the extract cannot be used without danger, as evidenced by the finding of areas of necrosis in the myocardium and the cortex of the suprarenal gland in animals which have received repeated injections of it.

[ED NOTE—The work of Hunter and Aub clearly demonstrates that continued administration of parathyroid extract causes increased elimination of calcium from the body and in time leads to decalcification of the bones.]

#### DEVELOPMENTAL DISEASES

*Osteochondritis Ischiopubica*—Attention has been called by Wuelfing<sup>9</sup> to a condition which he has named osteochondritis ischiopubica. The clinical picture resembles that of hip disease, although the symptoms are less severe. The condition consists of a disturbance of the ossification of the cartilage at the point of junction of the ischium and pubis in the acetabulum. An appearance of haziness and globular thickening develops. According to the author, the condition should be suspected when a patient complains of an indistinct disturbance of the gait, though on roentgen-ray examination the femoral head and the hip joint appear normal.

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7 Lehman, E. P., and Cole, W. H. Parathyroid Hormone and Calcification of Fracture Callus, *J. A. M. A.* **89** 587 (Aug. 30) 1927.

8 Hueper, W. Effect of Repeated Injections of Parathyroid Extraction on Calcification of Osteoid Tissues, *Arch. Path.* **3** 1002 (June) 1927.

9 Wuelfing, M. *Deutsche Ztschr. f. Chir.* **199** 413 1926.

cussing probable causes, they stated that acute or chronic infection or acute-intoxication, as in diabetes or gout, may be factors in rare cases. Nutritional diseases occurring about the age of 50 probably play an important part. Tobacco occupies a considerable rôle, while that of syphilis is insignificant. The writers do not regard Buerger's disease as a pathologic entity, but merely as a clinical form of endarteritis obliterans occurring with greatest frequency among the Jews of Central Europe.

Guillaumie<sup>30</sup> has made a study of the pathologic lesions in Buerger's disease, employing serial sections covering the entire length of the diseased arteries. As a result of his examinations he does not agree with Buerger's views, namely, that thrombosis constitutes the primary feature of the disease, with secondary parietal changes affecting the vessel walls. Guillaumie expressed the opinion that the primary lesion is a proliferating endarteritis which obliterates the lumen of the vessel and leads to thrombosis in the blind culdesac of the artery above that point.

*The Operation of Embolectomy in Embolic Disturbances of the Extremities*—Key<sup>31</sup> has performed the operation of embolectomy on ninety-five patients and is convinced of its value. In discussing his experience, he stated that the embolus is usually found at the point of division of an artery, and that if it does not at first completely occlude the vessel it quickly grows (from a few hours to several days) until it shuts off the blood supply entirely. To determine the seat of the embolus is difficult. Usually it is considerably higher than the region of circulatory disturbance. Palpation of the arterial pulsation may indicate the point of lodgment, but often the pulse is weak as a result of the weak heart. The diagnosis is easy when the embolus causes primary occlusion of the artery, but when the occlusion is only partial, it is much more difficult. Key found great advantage in local anesthesia, and advises that the operation be performed with this aid. He followed the technique of Carrell, using fine needles and sutures of silk sterilized in petrolatum. Gauze moistened with a 2 per cent solution of sodium citrate is used, and the instruments and gloves are rinsed in the same solution. The artery, after being compressed with a soft clamp, is opened somewhat above the point of suspected lodgment of the embolus. By careful traction even long emboli may be removed, but sometimes it is necessary to make a second opening in the vessel. When the embolus does not slip out easily, one must try to strip or massage it upward from below. The prognosis depends on the time elapsed between the lodgment of the embolus and its removal, the situation of the embolus and the general condition of the patient, especially the heart.

<sup>30</sup> Guillaumie, A. C. Bull et mem. Soc. med. d'hop. de Paris 51 611 (May 12) 1927.  
<sup>31</sup> Key, Ernst. Zentralbl. f. Chir. 54 2190 (Aug. 27) 1927.

*Osgood-Schlatter's Disease in Adults*—Opposing the opinion of other authors, Brandes<sup>10</sup> stated that Osgood-Schlatter's disease of the tibial tubercle occurs not only in young growing persons, but also in adults. He cited as an example the case of a man, aged 48, who showed the characteristic clinical signs and typical roentgenologic appearance. The symptoms dated from a strain received during the war. The examination showed that the apophyseal lines of the tibial tubercles of both knees had failed to ossify during the years of growth and had persisted as points of reduced resistance to strain. Brandes stated that he has seen a number of examples of the same condition in young adults of about 20 years. In the patients with only mild symptoms he usually found conservative treatment sufficient, but when the condition was persistent he employed operative treatment. The operation consisted in splitting the patellar tendon, exposing the tubercle, and removing the affected area with the curet.

[ED. NOTE—While symptoms may not arise until adult life, we do not believe that Brandes meant to infer that the condition originates then. The main fact is that Osgood-Schlatter's disease may go on in youth to complete failure of union between the apophysis of the tubercle and the tibia, and that the fibrous connection may yield to strain in later years. One of us has encountered this condition in young adults, and at operation found the tubercle entirely loose. Removal relieved the symptoms.]

*Vertebral Epiphysitis*—Zur Verth<sup>11</sup> has encountered in children a developmental disease of the spine that evidently corresponds to what other authors have described as vertebral osteochondritis. He found the condition limited to a single vertebra. In the early stage there is an appearance of marked atrophy of the vertebral body, with an irregular zone in the middle. In the later stage the body appears to diminish to a narrow plate which represents the central dense zone, while the adjacent areas disappear. The symptoms may resemble those of Pott's disease, but the author felt that he could exclude the possibility of tuberculosis, typhoid fever, syphilis, or trauma. He considers the condition to be related to Koehler's disease of the scaphoid and to other similar diseases, and proposes the name "vertebra plana."

*Clinical Importance of the Os Tibiale Externum or Accessory Tarsal Scaphoid*—Calling attention to the clinical importance of the os tibiale externum or accessory scaphoid, Sever<sup>12</sup> stated that this condition may be of medicolegal significance, especially following trauma, because of the possibility of its being mistaken for a fracture. It is generally associated with badly pronated and relaxed feet which are particularly

10 Brandes, M. *München med Wchnschr* 74 1830, 1927.

11 Zur Verth. *Ztschr f orthop Chir* 48 70, 1927.

12 Sever, J. W. *Clinical Importance of Os Tibiale Externum or Accessory Tarsal Scaphoid*, *J A M A* 89 359 (July 30) 1927.

*Treatment of Spastic Paraplegia by Sympathetic Ramisection*—Royl<sup>38</sup> reaffirmed his original opinion of the value of ramisection and described the late results of the operations he performed some years ago. Detending his experimental work, he wrote that "although a number of investigators have failed to verify my results, no one has attempted to reproduce them on the goat, the animal which I used." In the article, he repeated the story of his first operation on a patient, Sept 1, 1923. The improvement in this patient persists to date, three years after operation. Besides changes in tone, he enumerated the following results: In the first group he distinguished (a) cases in which the patient retained or had developed muscular control, (b) cases in which voluntary control was not present. He performed ramisection in twenty-six patients with spastic paraplegia of both lower limbs. All were of the rigid type except one of the choreic type. He analyzed his results as follows: Walking. There was diminution in disability in all but one patient. Before operation sixteen of twenty-six could not walk alone. Fourteen of these patients learned to walk within six months after operation. Changes in Tone. Rigidity invariably diminished and a wider range of movement developed. Balance. Increased facility in balance was an invariable postoperative result. Performance of Active Movements. "Almost every patient reported increased facility in performing active movements." Speed. Speed was always increased. Inhibition. Improved inhibition was a consistent result when the tone was great enough to impede normal movement. Changes in Condition of the Viscera. Seventeen of the patients were suffering from chronic constipation. Thirteen of this number "were more or less relieved." Vasomotor Changes. Every patient in the series exhibited postoperative vasomotor changes. The acute changes were transitory, but a definite increase in temperature and freedom from vasomotor disorder persisted after ramisection. In respect to structural changes such as contractures, the author stated that these must be dealt with surgically before the full effect of ramisection is apparent. In one patient who showed choreiform movements, improvement in function was definite and there was a lessening of the movements.

38 Royl, N. D. M. J. Australia 1 632 (April 30) 1927  
(To be continued)

resistant to corrective treatment. He has reached the point of view that in such cases when the feet are persistently painful, operative treatment is necessary. The operation consists of an arthrodesis of the astragaloscaphoid joint, with removal of the accessory scaphoid and shortening of the tendon of the tibialis posterior muscle.

#### NUTRITIONAL DISEASES

The chemical changes found in rickets have been discussed by Gamble,<sup>13</sup> who pointed out that the disease depends on a reduction, not only of the calcium in the blood plasma, but also of phosphorus. Since the calcium content is nearly stationary in ordinary rickets, the measurement of the phosphorus content of the blood plasma gives the degree of rickets. In tetany the blood calcium is materially lowered. The dietary studies have shown that an unknown substance "D" is necessary to keep the calcium and phosphorus balance up to normal. The same effect is produced by sunlight. This substance "D" is present in abundance in cod liver oil. He pointed out that from a practical point of view the important result of the recent studies of rickets has been the recognition of the curative action of cod liver oil and sunlight.

Hess<sup>14</sup> found that cholesterol when irradiated with ultraviolet light possesses antirachitic properties and that bran which contains a large amount of this substance may be used successfully. Ergosterol prepared from yeast is the only sterol found which acquires antirachitic activity on exposure. He stated that irradiated yeast may be used and that irradiated dried milk, the milk being the most successful.

Royal Rivers.—Scribn and Wilson<sup>15</sup> studied the case of a patient with renal rickets and reviewed the literature on this subject. The clinical picture in their own case corresponded to that of the cases reported by other authors and at autopsy showed typical changes. The symptoms in all cases have been similar, but the course of the disease and the development of the deformities have varied. In some cases the disease has been present at birth, in others it has developed later in life. In some cases the disease has been associated with other conditions, such as diabetes mellitus, and in others it has been associated with other conditions, such as hypothyroidism. The disease is characterized by a variety of symptoms, including bone pain, deformities, and in some cases, mental changes. The disease is caused by a deficiency of vitamin D, which is essential for the normal development and maintenance of the bones. The disease can be treated by the administration of vitamin D, either in the form of cod liver oil or of synthetic vitamin D preparations.

<sup>13</sup> Gamble, W. N.: *Biochem. J.*, 1925, 19, 1-10.  
<sup>14</sup> Hess, E.: *Ann. N. Y. Acad. Sci.*, 1925, 27, 1-10.  
<sup>15</sup> Scribn, R. L., and Wilson, J. H.: *Ann. N. Y. Acad. Sci.*, 1925, 27, 1-10.

## MÉNIÈRE'S DISEASE

ITS DIAGNOSIS AND A METHOD OF TREATMENT \*

WALTER E. DANDY, M.D.

BALTIMORE

The purpose of this communication is to present the results of an operation which I believe will permanently cure the symptoms of Ménière's disease. Briefly stated, the treatment is section of the auditory nerve intracranially. It is attended with almost no risk of life, and since there is always subtotal deafness on the affected side before the operation, section of the nerve adds little of practical importance to the deafness. Other symptoms do not result when the auditory nerve is severed.

In its usual form, Ménière's disease has a well defined and well recognized symptom complex. The patient is suddenly seized with a violent attack of dizziness, at once associated with nausea, vomiting and unilateral tinnitus referred to an ear which is progressively growing deaf. These attacks are repeated from time to time, usually with increasing frequency. The patients are well between the attacks, though eventually they may recur so frequently as to be almost continuous. At such times as to complain in case 1, the patient for weeks may not be able to take food or to retain it when it is taken. The attacks are of such violence and come on with such suddenness that the patient lives in terror of their reappearance. They last from a few hours to several weeks. The symptoms have been known and described for more than a century, but it was Ménière who first suspected their aural origin. Whether or not his impression proves to be correct he at least rescued a clinical entity from a hopeless confusion of symptoms which had not implied any pathologic significance. At the time of Ménière's publication the symptoms of this condition, and of epilepsy also, were considered evidence of cerebral congestion or apoplexy. Indeed the sudden nature of the attacks of Ménière's disease might well appear at first glance to be apoplectic.

It is necessary to understand the beliefs current at that time in order not to be misled by the title of Ménière's paper, 'Maladies de l'oreille interne offertes par les symptômes de la congestion cérébrale apoplectiforme'. There is even yet the erroneous impression (perhaps attributable to the

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Brockman<sup>16</sup> also reported his observations on three patients with the same condition. There was the same association of late developing bone deformities with chronic nephritis. He was able to obtain at autopsy a tibia and fibula from one of the patients for pathologic examination. The chief descriptive points obtained from this study are as follows: 1 The shafts of the bones in renal rickets are straight, and the deformities are due to separation and displacement of the epiphyses. (It is not desirable to correct the deformities because of the danger of uremia and the tendency to recurrence.) 2 The red marrow is replaced by fat marrow. 3 There is little bone formation. 4 Active bone absorption by osteoclasts takes place in the neighborhood of the growth disks and also of the shaft. 5 The absorbed bone is replaced by fibrous tissue. 6 The walls of the arteries in the medulla are thickened. 7 An increase in the number of capillaries is observed in the region of the growth disk.

*Osteitis Deformans*—Van Hazet and Andrews<sup>17</sup> made a study of osteitis deformans, or Paget's disease, with careful chemical and laboratory examinations of a group of patients. They recited briefly the history of the disease and the various theories concerning its etiology. Their own studies yielded the following results: 1 Chemical analysis of the blood and excreta showed that there was calcium retention despite a fall in the blood calcium. 2 An unusually rapid rise in the rate of absorption of sugar was noted. 3 The administration of epinephrine hydrochloride caused a decrease in the blood calcium. There was also a quick response of the blood pressure and a rapid return to normal. From this fact they concluded that in Paget's disease there is a polyglandular disturbance of internal secretion resembling parathyroid disturbance. They explained the pathologic picture as an increase in the permeability of the tissues entailing an inability of the osseous structure to retain calcium and the entire condition as due to a hypersecretion of the parathyroid gland.

#### ANATOMIC STUDIES

*Symmetry of the Bones in Fetal Life*—Koenig and Kornfeld<sup>18</sup> examined and measured the length of the bones in forty-two embryos and infants, and found that asymmetrical development of the bones, especially in respect to length, is common in fetal life, but generally disappears before or shortly after birth. The left clavicle and the left scapula are generally longer than the right clavicle and right scapula. The upper ribs on the left side also are usually longer. The relations between the length of the long bones of one extremity and of the bones of the leg to the bones of the arm change constantly during fetal life.

<sup>16</sup> Brockman, E. P. *Brit J Surg* **14** 634 (April) 1927.

<sup>17</sup> Van Hazet, Willard, and Andrews, Edmund. *Surg Gynec Obst* **45** 54 (July) 1927.

<sup>18</sup> Koenig, K., and Kornfeld, W. *Ztschr f d ges Anat* **82** 657, 1927.



title) that Mènière thought this condition was due to cerebral hemorrhage or to hemorrhage into the semicircular canals. He made it clear that the symptoms are considered by all authorities to be due to cerebral congestion, but he repeatedly emphasized his belief that they are surely due to a disease of the internal ear. Elsewhere he said "The signs of cerebral congestion, so called, are not too well established, and—the signs of cerebral congestion and apoplexy will have to be revised" in his paper Mènière referred to the work of Itard (published in 1825) in his paper At times, Itard is unjustly given credit for the discovery of Mènière's syndrome, but, according to Mènière he assembled cases of epilepsy, hysteria and other conditions with those of aural vertigo and classified all of them as "cerebral apoplexy." It is interesting that at the meeting of the Academy of Medicine of Paris when Claude Bernard was almost unanimously elected to be a member, the subject of cerebral congestion was discussed at length, and Mènière's work was cited as argument in opposition. It was the sense of the meeting that since "there was so much contradiction, confusion and exaggeration on this subject it was better to separate epilepsy and confine the attention to true cerebral congestion." Mènière maintained that there could not be any possible relationship between epilepsy and aural vertigo, because epileptic persons do not have unilateral deafness, and patients with aural vertigo do not lose consciousness nor have the mental stigmas so common to persons with epilepsy.

Mènière's belief in the site of the lesion in the disease which has since borne his name was largely due to the well known experiments on extirpation of the semicircular canals by Flourens (1842). Mènière also reported gross observations made at necropsy in one case with acute symptoms, which persisted until death occurred five weeks later. The semicircular canals were found to contain "serosanguineous lymph." The brain did not show any abnormality. The observations made at necropsy by Mènière are obviously those of some acute aural condition and are not those of Mènière's disease which is now known as a chronic disease. The necropsy report of Mènière cannot be used to support his clinical syndrome, unless it be to show that such symptoms may be present in an acute form and may be referable to a lesion of the inner ear and not to the brain.

There is, in fact, no available material to indicate the character of the underlying lesion of Mènière's disease. A few cases have been reported, but all are complicated by other lesions. Politzer's patient had a tumor of the brain, Volkmann's had meningitis, Gruber's patient died of typhus and had blood tinged lymph in the semicircular canals. Evidence that Mènière's disease is due to a lesion of the inner ear is based almost entirely on the presence of deafness. In the absence of proof, it is permissible to doubt that the pathologic process is actually in

*Mechanics of the Patella*—An investigation of the mechanics of the patella was reported by Moloney<sup>19</sup> He reached the following conclusions The patella is not a lever, and the femoral condyles do not constitute an efficient inclined plane The patella owes its efficiency to the fact that it increases the distance between the axis of rotation of the tibia and the line of direction of the force that pulls on the tibial tubercle by means of the patellar ligament

*Metatarsus Atavicus*—Under the term “metatarsus atavicus” Morton<sup>20</sup> described the condition in which the first metatarsal bone is shorter than the second The symptoms simulate those of other metatarsal disorders The diagnosis depends on the roentgenologic examination

#### CHRONIC ARTHRITIS

*Sulphur Metabolism*—Cawadias<sup>21</sup> made a study of the sulphur balance in persons with arthritis deformans, employing a method originated by himself The study included observations on thiopepy (that special metabolic function of the organism through which the sulphur equilibrium is maintained), sulphur oxidation, and sulphur conjugation He found a deficient thiopepy and increase in sulphur catabolism Sulphur oxidation was not disturbed and sulphur conjugation, in some cases, was increased He concluded that colloidal sulphur treatment may be of use in certain patients with arthritis

*Gastric Function*—Miller and Smith<sup>22</sup> made an investigation of gastric function by means of the test meal in a group of 250 patients with different types of chronic arthritis They found that the incidence of achlorhydria and hypochlorhydria in chronic arthritis was five times as great in their group of patients as in normal subjects Streptococci were isolated in 92 per cent of fecal cultures Both observations, while abnormal, do not differ from those encountered in a wide variety of other diseases, and, therefore, the authors concluded that these are not primary etiologic factors, but that achlorhydria may allow more ready multiplication of bacteria in the bowel and may be an accessory factor

*Basal Metabolism*—A careful study of the basal metabolism in 200 patients with chronic arthritis was made by Swaim and Spear<sup>23</sup> The patients were divided according to the classification of Goldthwait, Painter, and Osgood They found that age, duration of disease, and activity of the disease do not have any effect on the metabolic rate In the atrophic and hypertrophic types the tendency has been toward a minus rate In some of the patients, treatment by thyroid extract was attended by an immediate further drop in the metabolic rate As the

19 Moloney, J C J Bone & Joint Surg 9 476 (July) 1927

20 Morton, D J J Bone & Joint Surg 9 531 (July) 1927

21 Cawadias, A P Lancet 1 1283 (June 18) 1927

22 Miller, S, and Smith, F B Quart J Med 20 271 (April) 1927

23 Swaim, L T, and Spear, L M Boston M & S J 197 350 (Sept 1) 1927

the semicircular canals. In fact, by analogy with other conditions, it is easier to believe that the nerve itself and not the end-organ may be primarily involved. It is evident from histories of Meniere's disease that infections of the middle ear have no etiologic relationship. Meniere early called attention to the absence of otitis media and of hereditary factors in the explanation of an underlying case.

#### TREATMENT IN MENIERE'S DISEASE

Charcot (1874), who frequently demonstrated cases of Meniere's disease at his clinics, admitted the utter hopelessness of all forms of treatment then in vogue. He noted that when deafness became complete the disease stopped spontaneously. This observation prompted him to wonder if surgical intervention might not at some future time offer the solution by dividing the auditory nerve. But this suggestion was made when antiseptic surgery was just beginning and several years before the dawn of brain surgery. With one exception the attempts at surgical treatment have been directed toward the semicircular canals.

Frazier (1912), following a suggestion by Mills (1908), divided the auditory nerve intracranially in a single patient and precisely as in the operation here described, but the dizziness was not relieved. A study of Frazier's case leads one to doubt that the diagnosis of Meniere's disease was correct, the characteristic "attacks" of dizziness, nausea and vomiting were not present. Rather there was a chronic state in which dizziness could be induced by postural change. The patient also was unable to lie in comfort on the contralateral side. These symptoms would seem to indicate involvement of the cerebello—brain stem—vestibular paths by a neoplasm or inflammatory process. Furthermore, there was the history of influenza quickly followed by deafness—an etiologic relationship not recognized in Meniere's disease.

Section of the eighth nerve for persistent tinnitus was then tried by Frazier (1913), but the ultimate success is not known. He stated that "the intense roaring sound" had disappeared at the time of the patient's discharge from the hospital. The results in the cases reported in this paper make one wonder how far section of the eighth nerve can control noises referred to the ear.

Other surgical attempts at treatment in cases of Meniere's disease have been directed toward direct attacks on the inner ear after chiseling through the mastoid. Stoutant trephines the labyrinth. Fortnum makes the incus endolymphaticus. Aboulker exposes the duct behind the mastoid and expects to "decompress" the auditory nerve either with or without opening the duct. The assumption of Aboulker that an increase of pressure of the cerebrospinal fluid in the posterior cranial fossa was responsible for Meniere's disease was due to the fact that in that limited literature received the same terms. At present it is not clear



lobule (figs 13, 17, 18 and 24) The histologic structure of the parenchymatous portion of these nodules or areas was similar in all details to that characteristic of a lobule of hyperplastic parenchyma occurring in exophthalmic goiter (figs 12, 13, 20, 21, 22, 23, 26, 27, 28, 29, 30 and 31) The microscopic appearance of histologic regression and disinte-

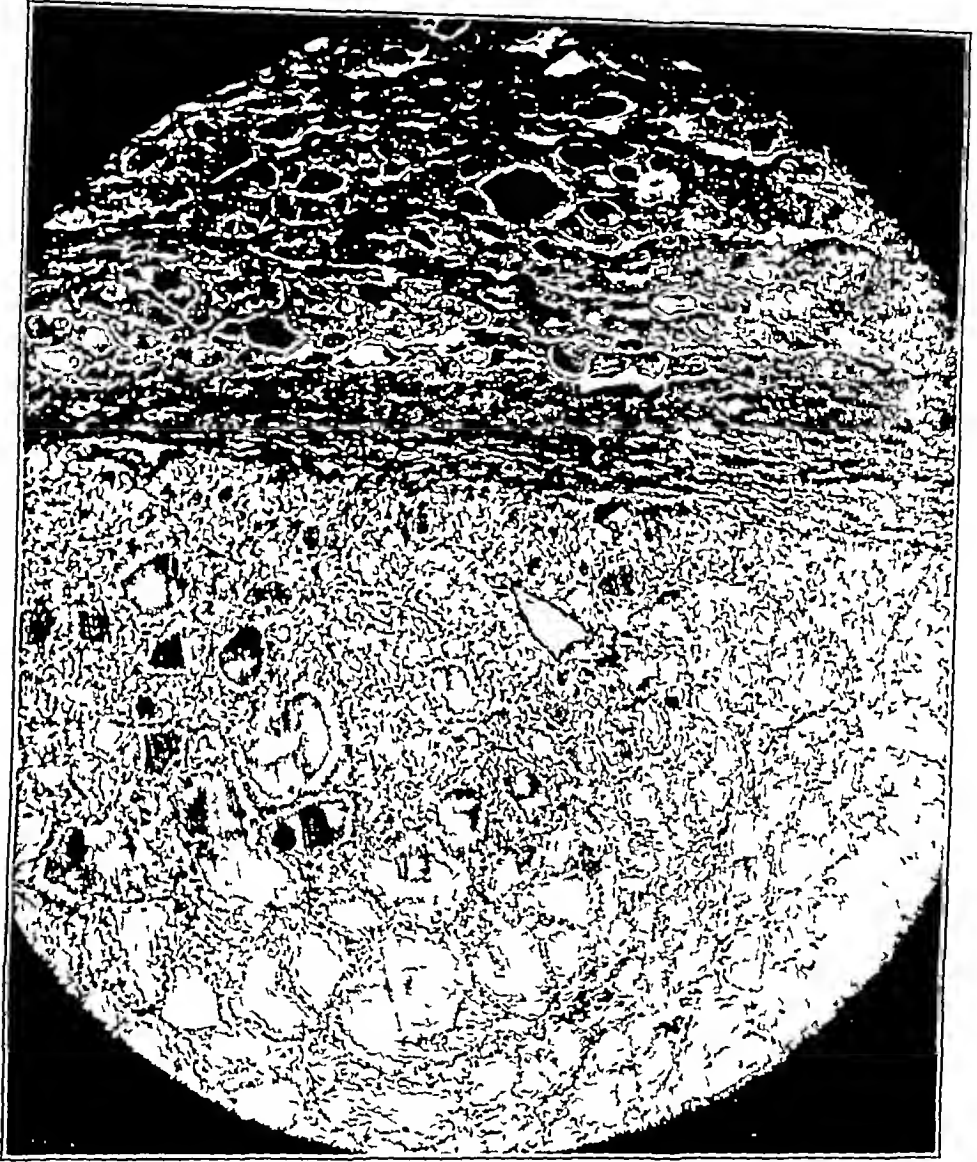


Fig 30—Section of tissue from tumor and contiguous tissue shown in figure 26 In lower half of section can be seen the typical microscopic pattern of hypertrophy and hyperplasia This tissue came from the tumor side The apparent capsule consists of compressed interlobular and intralobular septums between which atrophic acini can be observed In the upper portion of the section normal thyroid tissue can be seen Reduced from a magnification of  $\times 56$

gration with cyst formation noted toward the center of the areas was characteristic in every respect of the involutional changes observed and described as occurring throughout the gland as a whole following arti-

national Congress of Otology in 1922, this theory was supported by Nylen (Stockholm) and Quix (Utrecht). In refutation of this assumption it is only necessary to say that Meniere's disease is never seen when the intracranial pressure is really increased as in tumors of the posterior cranial fossa. An increase of pressure around one auditory nerve, aside from being pure conjecture, is impossible because the cisterna lateralis which surrounds the auditory nerve is freely open in three directions. In none of my operative series was there the slightest evidence of increased intracranial pressure, either local or general.

#### REPORT OF CASES

**CASE 1—History**—A well nourished man, aged 53, was referred by Dr. G. H. Barksdale, of Charleston, W. Va., in September, 1924, because of vertigo, nausea, vomiting and buzzing in the left ear. The symptom of the onset was a unilateral buzzing in the ear which began two and one-half years previously. Impairment in hearing was noticed at the same time and had progressed gradually. Two months before examination, a headache began in the morning, later in the day, the patient became very dizzy. He went to bed, but the vertigo continued throughout the day. There were severe nausea and persistent vomiting. Everything seemed to move to the left. He said that he believed he would have fallen to the left if he had not gone to bed. Other attacks occurred but they did not last longer than a day. Three days before admission he had the most severe attack which wakened him out of a sound sleep. He saw objects moving to the left, and was greatly nauseated for five hours. Numerous attempts to vomit were ineffectual. A friend who saw him in this attack said that the temperature was 97 F and the pulse rate, 60. For the past few months he had had a little headache over the occiput. The headaches were never severe, but were much worse during the attacks. Ringing in the left ear had been present since the onset of the condition. It was more intense during an attack. There had never been infection of the middle ear or mastoid.

**Neurologic and Physical Examination**—With the exception of a questionable positive Romberg test (with tendency to fall to the left) and the disturbance referable to the eighth nerve, the results of the neurologic examination were negative. The patient had a bradycardia (60) during an attack. The Wassermann reaction of blood was negative. According to the tests the hearing in the left ear was moderately impaired, a watch tick was not audible. C 64 was not heard in the left ear, C 128 was heard only one fourth of normal time. C 1024 and C 2048 were not greatly changed. Bone conduction was greater than air conduction.

Vestibular tests showed that spontaneous nystagmus was not present. There was a normal response to caloric stimulation of both ears, but the left ear (affected side) was more quickly induced than the right.

**Operation**—The left eighth nerve was divided intracranially under local anesthesia. The patient did not experience any sensation when the auditory nerve was dissected and divided. The postoperative course was uneventful.

Three and a half years after the operation, the patient was in perfect health and has been actively at work for the past three years. He has never had the slightest suggestion of an attack since the operation.

TABLE 1—Data Showing General

[illegible]

**CASE 2—History.**—A well nourished woman, aged 54 was referred to me by Dr Julian Chisolm, on Nov. 10, 1924. For three or four years the patient had had occasional attacks of dizziness and vomiting. At first they were not severe. One year before admission, she had a severe attack associated with ringing in the left ear and some impairment of hearing in the left ear. She was confined to bed for four days and found that she was much more comfortable when lying on the left side. Two months later, an even more severe attack prostrated her. It was like the preceding one, except that there was pain in the left occipital region and occasional tingling and numbness of both hands. There were also zigzag flashes of light. For the past three months before consulting me there had been a constant tinnitus in the left ear, some unsteadiness of gait and a constant dull ache in the region of the left mastoid. There was no history of otitis media.

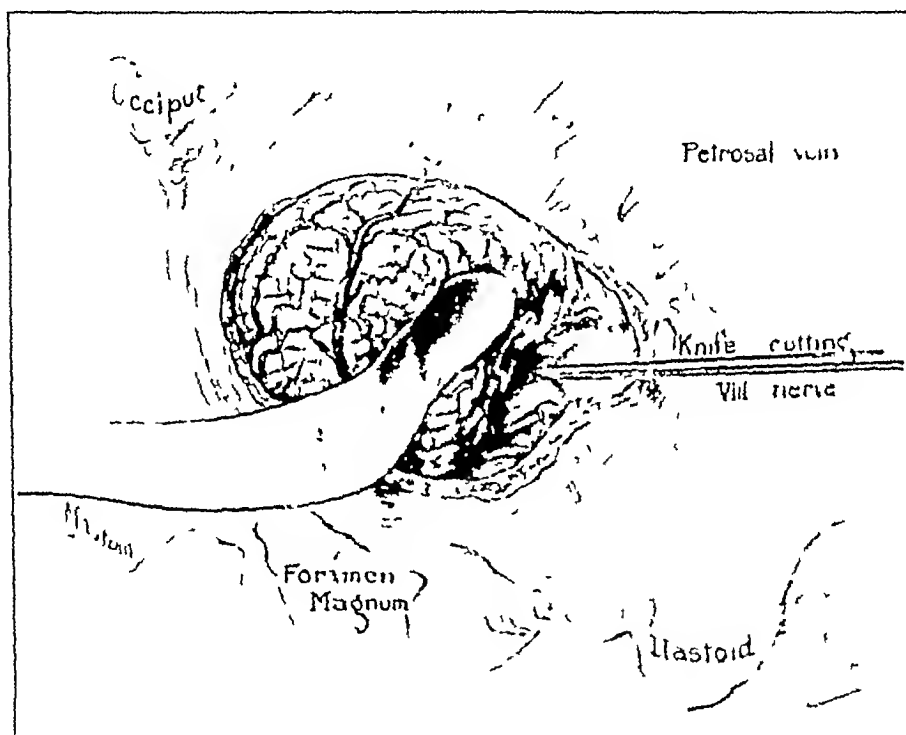


Fig. 1—Operative approach to region of the eighth nerve. The nerve can be divided either with a blade at right angles to a long shaft or with a small pair of scissors.

**Examination.**—The results of the physical examination and the Wassermann reaction of blood were negative. The results of the neurologic examination were negative, except for changes referable to the auditory nerve.

The hearing test revealed total deafness in the left ear; the right ear was normal.

The caloric test did not show any response to irrigations of the left ear; the right was normal.

**Operation.**—The left auditory nerve was sectioned intracranially on Nov. 12, 1924, under ether anesthesia. The patient was discharged from the hospital ten days later.

She has not had any attacks since operation. She complains of a dull, aching feeling in the occipital region at the operative field and a dull ache in





the eyes, this sensation has been present for more than twenty-five years. Sometimes there is a little dizziness with the flashes of light (migraine?)

**CASE 3—History**—An undernourished woman, aged 55, was referred by Dr Barker on Jan 11, 1927, because of Meniere's disease. She was exhausted from prolonged vomiting. Her skin was sallow and pale. Eighteen months before, she was suddenly seized with dizziness, nausea and vomiting. The attack lasted all night. The vomiting was described as projectile. She did not have any fever, chills or pain. She had never been well since the onset of the condition. Six weeks later, she had another attack precisely like the first.

The interval between attacks gradually lessened, until the patient was admitted to the hospital. Each attack lasted one or two days. Only hypodermic injections of morphine gave any relief. Six months before coming to the hospital, she had a prolonged attack during which she did not take food for five weeks. A diagnosis of gallstones had been made in her home town, and the gallbladder had been drained. Gallstones had not been present. The appendix had also been removed at the operation. Her attacks of dizziness, nausea and vomiting persisted as before, though possibly with some moderation. Five weeks before admission her most severe attack began and still persisted. Since the attack began, she had had scarcely any food. She said she felt as if she were going round, first one way, then another. The attacks were not brought on by change of position, but during an attack she could not lie on either side. Sudden movements of the head then intensified the attack. There had been a gradually progressive loss of hearing in the right ear since the onset of the present illness. At the time of consultation, she could hear but little on the right side. There was also a continual ringing in this ear which became much worse during attacks. Recently, there had been some ringing in the left ear. An occasional slight pain was experienced in the right ear. There had never been an infection of either ear or mastoid. Nothing in her past history appeared to have any bearing on her condition. An attack of rheumatism, localized to the right hip, was noted thirty-five years before. During the menopause, two or three years previously, cyanosis of the fingers had been noted. She had always been nervous. Since her trouble began (eighteen months before), she lost 26 pounds (11.8 Kg).

**Examination**—The patient was in Dr Barker's medical service for one month. There were few days during this time when the dizziness, nausea and vomiting were not present. The vomiting was often projectile. During most of this time she could retain nothing by mouth and was given fluids by rectal, subcutaneous and intravenous methods.

Except for the disturbed functions of the eighth nerve, the results of the neurologic examinations were entirely negative.

Examinations of auditory and vestibular functions were made by Dr Baylor. All tuning forks were heard on the left side within normal limits. On the right, there was marked shortening with all forks. Vibrations of tuning fork C 128 were barely heard to C 2048.

Irrigation of the right ear produced a rotary nystagmus to the left, but no subjective dizziness. Irrigation of the left ear caused a rotary nystagmus to the right, but no subjective vertigo.

The audiometer test showed loss of hearing in the right ear and of some of the high tones in the left ear. The vestibular function was not abnormal.

The Wassermann reaction of the blood was negative. The blood pressure was 110 systolic and 70 diastolic.

**Operation**—On Jan 11, 1927, intracranial division of the right auditory nerve was performed under local anesthesia. The patient was not conscious of any

cases there were losses of 18, 27 and 30 per cent in the good ears. These losses may or may not have any relationship to the other ear, which is the participant in Meniere's syndrome

One of the most surprising observations is the great variability in the results of tests of vestibular function. If Meniere's disease is really a primary lesion of the semicircular canals, it is fair to expect the vestibular function to be profoundly and uniformly disturbed, at least, it should be more disturbed than the auditory function. On the contrary, the acuity of response from caloric stimuli is found undiminished in three cases, and only slightly diminished in another

Three of the patients in the foregoing case reports had headache during the attacks. In two cases, the headache was on the side of the lesion and more in the occipital region than elsewhere. In another instance, the headache was general. One patient had a "queer" feeling in the head just before an attack. She looked on this as an infallible warning sign

One patient thought there might have been on one occasion momentary loss of consciousness. In none of the remaining cases was there a suggestion of loss of consciousness. The preservation of consciousness is indeed one of the striking characteristics of Meniere's disease. A distressing desire to urinate and defecate during an attack made it necessary for one patient to lie on the bedpan until the attack was over. Two patients complained of some general dizziness or "light headedness" between the seizures. In both of these cases the dizziness persisted for several months after the eighth nerve was divided, it gradually abated and in less than a year it had almost completely disappeared. Nystagmus, which is occasionally reported in cases of Meniere's disease, was not observed in any of the cases from this series

#### PSEUDO-MENIERE'S ATTACKS

The question has often been asked whether unilateral deafness is a necessary sign of Meniere's disease. Frankl-Hochwart suggested the term "pseudo-Meniere's" to apply to cases which seem similar but lack the unilateral deafness. The following history is presented as an instance of so-called pseudo-Meniere's disease because the attacks seem similar, yet without any subjective or objective evidence of impaired hearing, and no unilateral signs

A man aged 59, referred by Dr. S. J. Crowe, for the past eight or nine years had been having recurring dizzy spells associated with nausea and vomiting. During the attack everything whirled about him. He could not lie on the left side or on the back of the head. The attacks averaged about two a year. There was some tinnitus in both ears. At the onset of his trouble, attacks appeared almost daily for over a month gradually disappearing. Other spells lasted only a few days, but they were fearful, and he lived in terror of their reappearance. The whirling

sensation either when the auditory nerve was being liberated or when it was being divided. The postoperative course was uneventful.

Fourteen months after the operation, there had not been the slightest evidence of an attack. She had regained her original weight and more and was well.

**CASE 4—History**—A large robust man, aged 47, was referred in April, 1927 by Dr. F. C. Schreiber of Washington. One year before, the patient had felt dizzy when he awoke and raised his head. He vomited, but was not nauseated. He was bedfast for three days. He felt dizzy every time he moved his head and vomited nearly as often. It was three weeks before the dizziness entirely disappeared. Four months later, he had another attack exactly like the first but this lasted only a week. Seven months before, tinnitus and deafness developed in the left ear, both appeared suddenly during an attack of dizziness and vomiting. The attacks of dizziness were not associated with moving objects. Headaches were not present. The patient reeled and staggered when walking during an

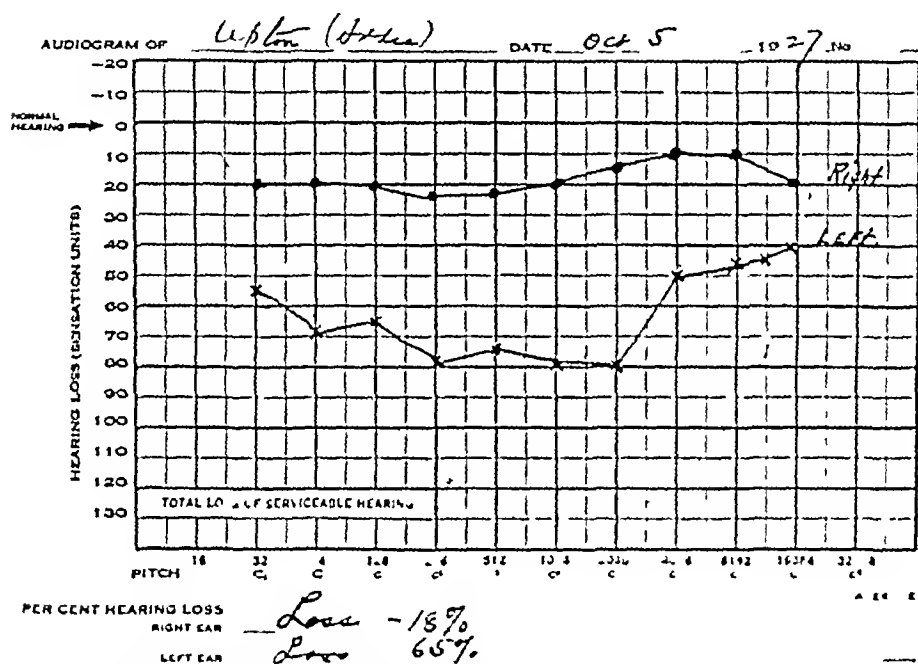


Fig 2—Audiometer chart showing the loss of hearing in a typical case of Meniere's disease

attack. During the past month, there had been no additional attacks, but the patient was always dizzy. He complained of poor memory during the recent attacks.

**Physical and Neurologic Examinations**—A positive Babinski sign and ankle clonus were present on the left side. The only other positive symptoms were the disturbed function of the eighth nerve. Unfortunately, the audiometer and caloric records of the functions of the vestibular and auditory divisions of this nerve were lost. It was recorded, however, that air conduction was less than bone conduction in the left ear and that hearing was best for the high notes and diminished for the low tones.

The blood pressure was 125 systolic and 85 diastolic. The Wassermann reaction of blood was negative.

The unilateral Babinski sign and ankle clonus made the diagnosis of Meniere's disease rather uncertain.

objects continued with his eyes shut but not so severely. Between attacks he was well in every way. Hearing was not impaired and there were no difficulties. The results of the physical and neurologic examinations were negative in every respect. Hearing tests were normal in both cats. Caloric tests gave normal response in both cats.

Although pseudo-Alzheimer's attacks are usually considered to be of hysterical origin, Politzer suggested that in some cases the organic character of disturbed hearing may be late in appearing. The analysis of my cases might seem to give support to this view for in three cases the loss of hearing (subjective) was not observed until long after the onset of the dizzy attacks. In the foregoing case however the attacks have been present for eight or nine years—far longer than the hearing-interval in any of my cases. The patient did not have any unilateral or bilateral attacks during the attack except that he could not lie on the left side or back of the head. Such a history would seem to preclude a hysterical attack. It is hardly possible that dizziness of this type could be simulated. Moreover, the patient is a practical, placid and unemotional person. The following report is from the most severe case of dizziness in my experience and differed from all others.

*I dæma (Fucphahins [?]) of Caribbium Producing I strong and I nourishing Dizziness. Ito Sore, Nausea and I vomiting—Hicor, —A well nourished woman aged 43, was referred by Dr HARRIS, Shick of Baltimore. For three weeks, she had been bedrrest with dizziness which is almost constantly present. It was least when she was on her back, became greatly intensified with every movement of the head to either side. Any attempt to raise the head off the pillow instantly brought on such intense dizziness that it prevented her she would pass into comat. She was almost always associated and vomited in my times. This illness came on suddenly and without an antecedent illness or infection. She complained of a feeling of pressure in the stomach and*

*Examination*—The results of the physical and neurologic examinations were normal. There was no detectable myasthenia. There was no disturbance of hearing in either ear. Chloric tests gave a normal response on both sides. Elevated rigidity was not noted. The temperature was never elevated. The cerebrospinal count was 13400 and 15800. Lumbar puncture was performed at 11 a. m. The pressure was subnormal, the fluid dropping only slowly. The rate of the examination was used by ingratia compression. Examination of the spinal fluid revealed there were 3 cells and no globulin. The Wassermann reaction of the spinal fluid was negative. The cerebrospinal fluid had been cleared of all bacteria. The spinal fluid was normal until the last four days when the counts became 13400 and 15800. The findings were mild and mixed.

[illegible]

*Operation*—In March, 1927, the left acoustic nerve was divided intracranially under local anesthesia. Thorough exploration of the cerebellopontile angle did not disclose a tumor. The entire intracranial course of the eighth nerve was in full view. Later, the symptoms did not clear up, and it was found by caloric tests that vestibular function was still present, though there was total deafness. Apparently, in an effort to avoid the facial nerve, the vestibular division of the nerve had not been divided. Two weeks later, the wound was reopened and this branch sectioned. The facial nerve was also injured despite caution. This was the only injury to the facial nerve in the series. It was later corrected by a spinofacial anastomosis.

The patient had not had attacks of dizziness and vomiting one year after the operation, but it is only fair to recall that for seven months prior to the operation he had had no attacks. After the operation he still complained of the constant dizziness which he described as lightheadedness and which was also present before operation. This steadily diminished after operation, until it was barely noticeable. The patient insisted that this dizziness was always worse in damp weather. It did not seem probable that it was caused by the disturbance of the eighth nerve, for it was unaffected by its section and seemed entirely independent of the attacks.

*CASE 5—History*—A well nourished man, aged 33, was referred to the hospital in June, 1927, because of dizziness. Two years before, he had suddenly become dizzy while at work. He continued at work but after an hour it was necessary to stop. A month later, a similar attack of dizziness had occurred while he was at work, and it had lasted all day. Nausea or vomiting were not associated with the attack. Objects always rotated from right to left, i. e., toward the deaf ear. During an attack he could not lie on the affected side, the dizziness was less when he was lying on the opposite side. At first the attacks recurred about every month, but there had been one free interval of seven months. During the past year there had rarely been an interval of longer than a week between attacks. In an effort to obtain relief, the nasal sinuses had been operated on, and the gallbladder had been drained. There were some left-sided headaches from the beginning, but they were always more intense just before an attack. A year and a half before admission, loss of hearing was noticed in the left ear, it had steadily progressed. Buzzing and ringing in the left ear had been present constantly for about the same length of time.

*Examination*—The results of the physical and neurologic examinations were negative, except for tests of hearing and vestibular function. The audiometer test showed a 58 per cent loss of hearing in the affected (left) ear and 27 per cent in the right ear. In the vestibular tests, caloric irrigations to the left ear did not give any response, they were normal to the right ear.

*Operation*—On June, 1927, under ether anesthesia, the left auditory nerve was sectioned at the internal auditory meatus. The patient had an uneventful recovery.

Ten months after the operation, there were no signs of recurrence of the attacks. There was occasional tinnitus.

*CASE 6—History*—A highly nervous, well nourished woman, aged 54, was referred by Dr. P. S. Sisco of Baltimore. For six years she was subject to violent dizzy spells which came on without warning and were accompanied by nausea and vomiting. The duration of the attacks varied from a few minutes to eight hours. During the attack she was afraid to move, for any change of position exaggerated her symptoms. Her first attack had occurred when she awoke from a sound sleep. Objects moved from left to right, i. e., away from the lesion. The

cranial fossa—was obliterated. The tonsils of the cerebellum had herniated into the spinal canal completely filling the foramen magnum. To liberate them, the dura was split in the midline to the atlas. The lateral ventricle was tapped in an effort to decrease the pressure, but there was no hydrocephalus. The cerebellar lobes were equal in size and looked alike, both appeared much smaller than normal. There was no apparent cause of the great pressure. There was no surface appearance of a tumor, and the short duration of such fulminating symptoms seemed to make the presence of a tumor unlikely. An extended search was not made for a tumor. There was no evidence of an inflammatory process. It was difficult to close the muscles owing to the pressure. A bilateral cerebellar decompression remained and constituted the only therapy resulting from the operation. The dizziness at once disappeared and had not returned one year after operation. It is also noteworthy that after the operation the patient could lie in any position without inducing dizziness.

*Comment*—The swelling of the cerebellum was undoubtedly due to edema, but the cause of the edema remains obscure. A few months after the operation the decompression was soft and did not protrude. The swelling of the brain, therefore, must have subsided. If a tumor had been present, the decompression would have become progressively tighter. Perhaps in the absence of any recognizable cause the lesion may be considered a form of encephalitis. The cerebellar edema does not suggest in any way angioneurotic edema described by Oppenheim as a not uncommon cause of Mènière's disease. The absence of increased pressure by spinal puncture was due to the fact that the cerebellar tonsils had filled the foramen magnum and prevented the transmission of cranial pressure. The symptoms in this case differ from Mènière's disease in the constancy of the symptoms and the absence of attacks with associated deafness. They differ from pseudo-Mènière's also in the absence of attacks. The symptoms are associated with organic cerebellar lesions, which will be considered shortly.

#### MÈNIÈRE'S ATTACKS DUE TO A LOCALIZED LESION ON THE AUDITORY NERVE

That attacks with the characteristic symptoms and signs of Mènière's disease may be due to a localized lesion involving the auditory nerve is shown by the following case report

*History*—A rather feeble woman, aged 66, was seen in consultation with Dr. Leslie Gay of Baltimore. Her first symptoms were gradually progressive deafness and tinnitus of the left ear (the right ear was almost deaf from an old infection during childhood). One year later she was suddenly and without warning seized with a terrific attack of dizziness during which there was nausea and repeated vomiting. The room seemed to jump around, the bed to tilt up and the walls to move in every direction. There was no definite revolving sensation. The attack lasted about thirty minutes. Brief spells of much the same character have since occurred almost daily. Any quick movement will induce dizziness. The deafness varied greatly from time to time. Tinnitus was constant in the left ear. Her eyesight became so poor that she could not read. She never had headache.

attacks averaged two or three a month. Vomiting was persistent and exhausting. There was also a distressing desire to micturate and defecate and since she lay motionless to reduce the dizziness as much as possible she had to remain on the bedpan throughout the attack. After a seizure she fell asleep, and on awakening felt well again. The attacks had greatly increased in frequency until she had several each day. A gradual loss of hearing in the left ear had occurred until she thought she was totally deaf on that side. The other ear had not been affected.

She said that for about a year she staggered like a drunken person but without a definite tendency to fall to either side. During the past month she had felt



Fig. 3—Scar after operation at which the eighth nerve was sectioned intracranially for Meniere's disease.

dizzy almost constantly. Recently any sudden motion of the head precipitated an attack. For years she had been unable to lie on the affected (left) side. Tinnitus—a ringing noise—had been present in the left ear since the onset of the condition six years before. She thought her memory was affected. Occasionally before an attack she noticed that everything seemed bright but she did not see a definite visual aura. She also had a vague impression of feeling "red" before an attack but she could not give any better description of the feeling. There was no history of otitis media.

*Pathology*—The results of the physical examination were negative. Wassermann reaction of the blood was negative.



Her systolic blood pressure varied greatly during Dr Gray's observations over a period of several months. Usually it ran from 160 to 190, but has been as low as 110. Her hands and feet were swollen at times, even when in bed, it will be remembered, the swelling was absent.

One month before operation her symptoms became much more severe. Rotting was nearly always present throughout the head, and was often restricted to both ears. The hearing became much worse. Her gait was mislaid and uncertain. The left corneal reflex was diminished.

Caloric response on affected side was normal. Irrigations started mild attacks of dizziness and nausea.

The auditorium test showed 63.5 per cent loss of hearing in the right ear (old deafness), and 65 per cent loss in the left (affected side).

*Operation*—On Nov 22, 1927, a section of the left auditory nerve was performed. An aneurysm was found under the eighth nerve. It was traced downward and was continuous with the vertebral artery. Two days after operation, the old noises returned. One week later, it was noted that she could not lie on the left side (nerve cut on this side) for any length of time because nausea and vomiting would start, but dizziness had not been present since operation. The patient's condition became slowly worse and the noises became unbearable. She was unable to stand. Three weeks later, the left vertebral artery was tied in the neck. At the same operation, the right vertebral artery was exposed and punched between the blades of the forceps, death resulted apparently simultaneously and instantly. Immediate release of the forceps was unnecessary.

This case is presented as an illustration of a tumor (aneurysm) pressing on the eighth nerve and giving symptoms which, until later neurologic symptoms appeared, did not seem different from those of true Almer's disease. It will be noted also that the basal aneurysm was so situated that the vestibular function was not affected, at least as far as indicated by caloric tests. The case also illustrates the fact that a primary lesion of the semicircular canals or of the cochlea is not necessary for the induction of attacks of the Almer's type and that a lesion of the nerve itself and more specifically of the cochlear branch alone can cause them. I am reminded of the analogy with trigeminal or glossopharyngeal neuralgia, in which in their usual form a systematic cause is not demonstrable, but occasional cases are attributable to tumor and are not different from the same primary neuralgic pains.

Another point is brought out in the analysis of the same series, namely, that while in most of the cases the worms had to be put in a jar of water, in the case of the *Ascaris* and *Ascaris* worms, a small amount of water was sufficient to keep them alive.

The results of the neurologic examination were negative, with the exception of the changes referable to the eighth nerve

The hearing test showed a 70 per cent loss of hearing in the left ear and 30 per cent in the right

The left ear did not show any response to the caloric test, the right ear was normal

*Operation*—On Aug 16, 1927, the left eighth nerve was divided under ether anesthesia

The patient left the hospital ten days later Eight months after the operation, she was well and had had no sign of her old attacks Only an occasional trace of tinnitus remained

*CASE 7—History*—A woman, aged 35, was referred by Dr T P Sprunt of Baltimore in April, 1927, because of attacks of dizziness Ten years before a thyroidectomy had been performed by Professor Halsted because of marked symptoms of exophthalmic goiter She had never been in robust health since the operation, but she had continued to work steadily and had not had any serious illness

She dated the onset of her condition to a sudden attack of dizziness fifteen months before when she was about to leave home She had a violent sensation of turning to the right Shortly afterward she was nauseated and vomited The attack wore off during the day Since then, similar attacks had occurred rather frequently, until she had them about every two or three weeks The dizziness never caused her to reel or fall, but there was the sensation that she was rotating to the right, i e, away from the lesion The symptoms were accentuated when she lay on the left side As long as she kept still and kept her eyes closed, she was much better Between the attacks she was free from any disturbance Since the beginning of her dizziness, the hearing in the left ear had been impaired This had been progressive Tinnitus was present almost constantly throughout her illness, but was worse, perhaps, at the time of the attacks Her past history did not shed any light on the cause of her illness She had never had otitis media or mastoiditis The blood pressure was 128 systolic and 82 diastolic The Wassermann reaction of the blood was negative.

*Examination*—The results of the physical and neurologic examinations were negative, with the exception of the local alteration in the function of the acoustic nerve

The audiometer test showed a 56 per cent loss of hearing in the left ear, the right was normal The caloric tests showed a normal response in both ears

*Operation*—The left auditory nerve was divided intracranially under local anesthesia When the acoustic nerve was being manipulated and divided, the patient complained of the same sensation of rotation and of nausea as during an attack It promptly disappeared when the nerve was severed The postoperative recovery was uneventful

One year after the operation, the patient had not had any sign of her former attacks For several months, she had had a feeling of dizziness and uncertainty when walking and was hesitant about crossing the street This has now disappeared almost entirely The noises in the ear persist as before They have become less noticeable as she pays less attention to them It is my impression that the tinnitus is neurogenic

*CASE 8—History*—A well nourished woman, aged 32, was referred from the medical dispensary Five years before she was suddenly seized with a severe attack of dizziness accompanied by severe nausea and vomiting She felt as

TABLE 2—Analysis Showing Different Kinds of Diagnosis in Menière's Disease

Patient	Location of Tumor	Kind of Tumor	Patient On Life in Comfort on		Dizziness Made Worse by Lying on the		Does Movement of Hand Precipitate Dizziness		Do Objects Turn	Is Onset Patient's Sudden or Gradual	Are Attacks Accompanied by				Hearing	Remarks
			Side of Lesion	Opposite Side	Side of Lesion	Opposite Side	Back	Yes			Tinnitus	Nausea	Vomiting	Caloric Test		
1	Aneurysm of basilar artery	Aneurysm	No	+	+	Im proved	Im proved	No	Yes	Turn	Sudden	+	+	+	68% loss, but varies from day to day	Outing stopped dizzy spells but did not stop tinnitus and old noises in ear, diminution of left ear, neural reflex, blood pressure varies from 110 to 100 gait finally became unsteady, though unaffected at first
2	Left lobe of cerebellum to the left of the center	Sarcoma	No	+	+	Im proved	Im proved	No	Yes	Turn	Sudden	+	+	+	68% loss, but varies from day to day	Outing stopped dizzy spells but did not stop tinnitus and old noises in ear, diminution of left ear, neural reflex, blood pressure varies from 110 to 100 gait finally became unsteady, though unaffected at first
3	Right lobe and vermis	Gloma	No	+	+	Im proved	Im proved	No	Yes	Turn	Sudden	+	+	+	68% loss, but varies from day to day	Outing stopped dizzy spells but did not stop tinnitus and old noises in ear, diminution of left ear, neural reflex, blood pressure varies from 110 to 100 gait finally became unsteady, though unaffected at first
4	Right cerebellopontile angle and fove	Gloma	+	+	+	Im proved	Im proved	Yes	Yes	Turn	Sudden	+	+	+	68% loss, but varies from day to day	Outing stopped dizzy spells but did not stop tinnitus and old noises in ear, diminution of left ear, neural reflex, blood pressure varies from 110 to 100 gait finally became unsteady, though unaffected at first
5	Right extra cerebellar	Sarcoma	+	+	+	Im proved	Im proved	Yes	No	Turn	Sudden	+	+	+	68% loss, but varies from day to day	Outing stopped dizzy spells but did not stop tinnitus and old noises in ear, diminution of left ear, neural reflex, blood pressure varies from 110 to 100 gait finally became unsteady, though unaffected at first
6	Left cerebellar lobe	Small tubercle 1.5 by 1.5 cm	No	Im proved	+	Im proved	Im proved	Yes	Yes	Turn	Sudden	+	+	+	68% loss, but varies from day to day	Outing stopped dizzy spells but did not stop tinnitus and old noises in ear, diminution of left ear, neural reflex, blood pressure varies from 110 to 100 gait finally became unsteady, though unaffected at first
7	Right cerebellopontile angle	Gloma	No	+	+	Im proved	Im proved	Yes	Yes	Turn	Sudden	+	+	+	68% loss, but varies from day to day	Outing stopped dizzy spells but did not stop tinnitus and old noises in ear, diminution of left ear, neural reflex, blood pressure varies from 110 to 100 gait finally became unsteady, though unaffected at first
8	Right temporal and occipital lobes	Cyst with intracystic angioma	+	+	+	Im proved	Im proved	Yes	Yes	Turn	Sudden	+	+	+	68% loss, but varies from day to day	Outing stopped dizzy spells but did not stop tinnitus and old noises in ear, diminution of left ear, neural reflex, blood pressure varies from 110 to 100 gait finally became unsteady, though unaffected at first

though she were 'falling forward or backward,' and it was necessary for her to hold on to something to keep from falling. The next attack occurred three weeks later. Since then, the attacks had recurred with increasing severity and greater frequency, until they averaged about two or three a week. The attacks occurred without apparent cause and were not induced by movements of the head or body, they often occurred when the patient was sitting or recumbent. Objects moved before her but with indefinite direction, they seemed to whirl in a general confusion. Three years later, she first noticed that the hearing in the left ear was impaired, this progressed until she was practically deaf in that ear. There was no tinnitus. Recently, there were some dull frontal headaches, but they were not important. She said that occasionally, during the most severe attacks, she thought that she lost consciousness, momentarily, and that she had a tendency to stagger to the right during the dizzy attacks, during the free intervals, the gait was normal. Later a new feature was added to the attacks, in that there was a 'queer feeling' in the head just before the attack began. She took this as a warning signal to lie down promptly. There was no history of otitis media or mastoiditis and no known cause for her distress.

*Examination*—The results of the physical and neurologic examination were negative except for the local condition.

The hearing tests showed a marked reduction of hearing for all tones in the left ear. Air conduction was greater than bone conduction. Hearing on the right side was essentially normal, there was about 65 per cent loss of hearing on the left by the audiometer test and 18 per cent on the right.

In the caloric tests, irrigation of the left (affected) ear with ice water caused rotary nystagmus. The response of the right ear was more active.

Dr. Crowe had observed this patient for more than a year, and had made several audiometer examinations. The tests showed a steady increase in deafness.

*Operation*—The left auditory nerve was divided intracranially under ether anesthesia. The postoperative course was uneventful. Four months after the operation, there had been no suggestion of an attack. It is worthy of note that one year before the operation, the eighth nerve was explored and an anomalous artery lying on the nerve was "clipped." A unilateral decompression resulted. No improvement followed.

*CASE 9—History*—A greatly undernourished woman, aged 47, was referred by Dr. J. Heyward Gibbes of Columbia, S. C., on Jan. 2, 1928. Five years before, she was suddenly seized with an attack of dizziness while walking. She did not fall, but probably would have done so if she had not sat down. She was nauseated and vomited. Since then similar attacks, lasting from three to five hours, had occurred every few weeks, but not infrequently they had occurred every two or three days. After many spells she remained very weak for several days; at times it would require two weeks to recuperate. During the attack everything seemed to be turning around from right to left, i. e., toward the affected side. She could lie comfortably only on the back or her head. There was one free interval of six months, and for the past nine months nausea and vomiting had been absent during the attacks. She fell during three attacks. She said that the attacks occurred so suddenly that she fell before she realized it as dizziness. The seizures varied considerably in severity. Diminution of hearing was first noticed in the left ear at the time of the first attack. The hearing gradually diminished, until she was practically deaf in that ear, but the hearing was unchanged on the other side. Tinnitus had been present at intervals in the left ear since the first attack of dizziness but was never present in the right ear. She described the sensation as a "pulling" or "dragging" sensation, as if

head In other words, the real difference, if any, between the dizziness in the attacks of Ménière's and that of tumors in the cerebellum and brain stem, need not be great, for one type of dizziness can seemingly merge into the other and either may be induced by the same lesion

#### OTHER TYPES OF DIZZINESS FROM KNOWN LESIONS

In order to compare the dizziness during an attack of Ménière's disease with that associated with other known lesions of the brain, and to determine if possible the significance of differing kinds of dizziness, the analysis in table 2 has been made

It will be seen that seven of these lesions are located in the posterior cranial fossa, only one was found in the right temporal and occipital lobes It was formerly my impression that if severe dizziness, nausea and vomiting are induced or greatly accentuated when the position of the head is changed, or if the patient is practically unable to lie with the head in certain positions, the lesion, whatever its character, is probably located in the posterior cranial fossa The fact that this is not absolutely true is shown by case 8 in which the lesion is exclusively cerebral, but there is no doubt that tumors and other lesions in this general region produce dizziness as a symptom much more profoundly and in much more distressing form than tumors located in the cerebral hemisphere

I had hoped that such a striking symptom as the inability to lie on one side without starting dizziness or without making it worse and the relative or complete immunity from dizziness by lying on the other side might prove to be a valuable localizing sign, or at least indicate the side of the lesion But this does not appear to be true From the patients in whom this character of the dizziness has been analyzed and checked with the strictly unilateral lesions, it will be seen that three could lie with comfort on the side of the lesion but could not lie on the contralateral side, and five (one cerebral) could lie in comfort on the contralateral but not on the ipsilateral side One must, therefore, conclude that this symptom has no importance in deciding the side of the lesion I believe, however, that this type of dizziness is a most important indication that an organic lesion—a tumor or inflammatory process—does exist in or on the cerebellum or brain stem and possibly certain parts of the cerebral hemispheres Dizziness does not seem to be different whether tumors are within or without the brain stem and cerebellum When dizziness is present, there does not appear to be any special feature to differentiate that in Ménière's disease from the dizziness associated with tumors of the cerebellum and brain stem, or perhaps of the cerebral hemisphere In any of these conditions objects or even the person may move, and in either case change in position of the head may increase the dizziness On the whole the dizziness, nausea and vomiting are much more fulminating and profound in Ménière's disease Moreover, Ménière's is character-

whistle It was always worse after a dizzy attack. She did not think that the hearing was worse after the spells Headaches did not occur She had not had otitis media

*Examination*—The results of the physical examination were negative The Wassermann reaction of the blood was negative

The neurologic examination showed the following positive symptoms The left corneal reflex was greatly diminished, the Romberg sign was positive, the patient falling to the left Left facial weakness (but doubtful) was suggested by the fact that blinking seemed a little tardy There was no ataxia or adiadochokinesis The eyegrounds were normal

The audiometer test showed 90 per cent deafness in the left ear Bone conduction was absent for tuning forks 128 to 512 Hearing in the right ear was normal Weber's test referred to the right ear

The caloric test did not show any subjective or objective response whatever on the left, the right ear was normal

The absence of response to caloric stimulation, the positive Romberg sign and the diminished corneal reflex made me entertain the diagnosis of a cerebellopontile tumor, though the character of the attacks seemed more like Meniere's disease

*Operation*—Cerebellar exploration was performed on Jan 4, 1928 There was no tumor in the cerebellopontile angle The auditory nerve was clearly visible from the pons to the internal auditory meatus There was no sign of pressure in the posterior cranial fossa The auditory nerve was divided

The patient made an uneventful recovery and was discharged two weeks after the operation There have been no attacks to date (three months after operation) The patient wrote that she was in better health than for many years Occasional tinnitus occurred

#### SYMPTOMS AND DIAGNOSIS OF MENIERE'S DISEASE

There has not been the semblance of an attack since operation in any of the nine cases There was reason to question the cure by the operation in only one case (2) This patient is the only one of the nine who had total loss of both vestibular and auditory function (at least to our tests) at the time of the operation It is, therefore, open to question why she had attacks if the nerve was totally out of commission We are thrown on two possible explanations (1) that some slight nerve function might still have been present and have evaded the tests, or (2) that since the last attack before operation the deafness had become complete, and if this were true, the cure should and might well have been spontaneous and not dependent on surgical division of the nerve

It may be asked how it can be certain the nine cases are Ménière's disease The diagnosis was made on the objective symptoms of unilateral subtotal deafness, and in each instance, inspection of the entire intracranial course of the auditory nerve excluded a tumor or other localized space-occupying lesion Perhaps the most important single diagnostic feature of Meniere's disease is the sudden, fulminating onset of "attacks" without warning and without recognizable inciting cause, and after the attack has subsided, the patient is again in perfect health with

the hearing never returns. An artificial cleavage between the two branches of the nerve, if attempted, must, therefore, be made with the least possible trauma.

#### IS MENIERE'S DISEASE "AURAL" VERTIGO?

Grouping of symptoms into a syndrome without an underlying pathologic basis always carries much uncertainty and a burden of proof. On the one hand, it is possible that the same symptoms may be attributable to different causes and on the other hand, different symptoms may have the same underlying cause. It is difficult to know on the basis of what particular symptoms cases may be included or excluded from Meniere's disease.

Apparently no case of Meniere's disease in its chronic form has been subjected to careful pathologic studies after death. This being true it is permissible to doubt that Ménière's disease is really "aural vertigo." There are certain data which at least make it probable that a lesion of the semicircular canals is not the cause. It cannot be reasoned that the lesion is primary in the semicircular canals because movements of the head stimulate dizziness. The examples, par excellence, that dizziness need not be from this source are given in the cases of dizziness due to verified tumors of the brain and allied lesions in the cases already reported. In these cases changes in posture induce dizziness and here the semicircular canals are known not to be involved. Probably stimulation of the semicircular canals induces the dizziness, but the source of the stimulus is elsewhere. It is known to be at a distance and in the nervous pathways, *i. e.*, the cerebellum, brain stem and auditory nerves. These pathways together with the internal ear form a system which when working properly controls equilibrium, and when disturbed induces dizziness. That the semicircular canals do not harbor the primary lesion of Ménière's disease is also strongly indicated by the fact that in one third of the cases reported in my series there was no appreciable alteration of vestibular function as tested by the caloric reaction. I have not felt justified in using other tests of presumed vestibular function, such as the rotation experiments, because of the patient's great dread of inducing attacks.

On the other hand, it may be reasoned that the cases of so-called pseudo-Ménière's disease are precisely like those of true Ménière's except that unilateral deafness is absent, and that in these cases the primary lesion is probably in the semicircular canals and not in the cochlea. Against this argument is the absence of any change in the caloric reactions in the foregoing case. Cases in which there is loss of vestibular function with cochlear function unimpaired have not yet been demonstrated. However in the absence of positive objective evidence, the location of the offending lesion cannot be assumed.

only a residual unilateral loss of hearing and persisting tinnitus. It will be seen from table 1 that while there are differences in detail, the general character of the attacks is much the same. Dizziness and unilateral tinnitus are the only two absolutely constant symptoms in the cases of this small series. In one patient nausea and vomiting were absent in all attacks, and in another, the nausea and vomiting, though present in early attacks, later disappeared. The character of the dizziness varies. Usually but not invariably objects rotate or whirl. Objects may seem to turn in one direction as in case 1, to the left, they may turn first one way then another (case 3), or in no definite direction (cases 7 and 9). In one case (7), the patient seemed to be turning to the right, and in another case (3), she seemed to revolve first one way then another. It is interesting to note that in three cases objects seemed to rotate toward the affected side and in two toward the opposite side.

During an attack, movements of the head intensified the dizziness in all cases. In one case increase of symptoms resulted from the movement of the eyes so that the patient had to keep her eyes shut during the seizure. Nearly all patients are at once forced to seek the recumbent position. One patient dared not move from the flat of her back or turn her head until the attack had worn off. Two other patients could not lie on either side and obtained relative freedom only when lying on the back of the head. One patient was not conscious of any difference in symptoms owing to position. Without exception movements of the head or body failed to induce dizziness after the attack had passed though one patient always slept on the opposite side because she feared an oncoming attack.

Tinnitus was uniformly present and always in the affected ear. In one case (8), however, it did not appear until five years after the onset of the attacks and even then was a minor symptom. Usually it persists in the free interval between the attacks. At times intensification of the tinnitus seems to usher in an attack and is worse during and for sometime after the seizure has passed. Tinnitus is described as a ringing or buzzing sensation. In one case, tinnitus did not develop until six months after the first attack and was synchronous with deafness.

Hearing was diminished in one ear in every case usually to the point of rendering the ear almost useless for practical purposes. In recent cases in which audiometer tests were made the loss of hearing was 75, 65 and 90 per cent. It is noteworthy that although the loss of hearing was noticed synchronously with the first attack this is not always true. In case 2 deafness was not noticed until two years after the first attack, in case 4 five months, and in case 8 three years after the first attack. It is of course possible that the earliest stages of deafness were not observed by the patient. But when the first attack occurred deafness was present in only one ear. In the three cases in which audiometer tests were made the losses of hearing were 50, 65 and 75 per cent. In the



ized by "attacks" and in the free interval the patient is almost symptom free, whereas from tumors a more or less chronic state of dizziness exists, or at least the patient remains in a potential dizzy state. In true Ménière's disease there is an associated loss of function of the auditory nerve, and this does not obtain in tumors unless this nerve is directly compressed as was true in two of the foregoing cases or in occasional cases of cerebellopontile tumors.

It is in the cases of direct involvement of the auditory nerve by tumors that the differential diagnosis from Ménière's disease becomes more difficult. In the later stages of a tumor's growth there are other signs of pressure and of contiguous nerve involvement making the diagnosis easy, but in the earlier stages these manifestations are absent. In neither of the two cases just mentioned were there signs of pressure or of implication of other cranial nerves. On the other hand, in one of the reported cases of Ménière's there was a positive Romberg sign and a diminished corneal reflex, both presumptive signs of a tumor, but a tumor was not present. In another case there was a positive Babinski sign and ankle clonus on the side of the deafness, but seemingly neither was significant. One of the important features of the operation here described is that a tumor if present will be disclosed and if not present the only alternate diagnosis would seem to be Ménière's disease, and for this section of the eighth nerve is the rational treatment.

At times one is confronted by Ménière's disease affecting the only good ear. A case in point was seen by me several months ago and was recently explored. There was some variation from the usual story of Ménière's disease in that the hearing varied greatly from time to time, often suddenly and without apparent explanation. On the chance that a gross lesion might account for this phase of the symptoms—the basilar aneurysm heretofore referred to gave a similar story and was in fact the only case of either series with such variation in hearing—the nerve was explored but there was no tumor. Since it did not seem justifiable to sacrifice his hearing, the auditory nerve was not divided.

In one of the patients from this series, the vestibular and cochlear branches of the auditory nerve were separate and distinct, such an anatomic variation would lend itself to division of the vestibular nerve without injuring the cochlear nerve and the hearing. Even when the two branches are inseparable, an artificial though necessarily inaccurate division should easily be possible with preservation of at least the major part of the cochlear branch. Such a procedure was contemplated but was not carried out in the patient who was deaf in the other ear. Perhaps it may yet be advisable though there is no precedent on which a cure could be assured. Other experiences have shown how sensitive the auditory nerve is to trauma and even though the injury seems slight,

focal and spontaneous remission in cases of exophthalmic goiter (figs 19, 20, 21, 22, 23, 24 and 27). The microscopic structure appeared to be that of a localized area of the parenchyma of the thyroid which presented the histologic changes characteristic of hypertrophy and hyperplasia associated with a supervening exacerbation but in this lobule there could also be seen the histologic regression and scarring characteristic of involutional changes which had occurred during a previous remission. These nodules or localized areas of hypertrophy and hyperplasia had apparently become encapsulated as a result of compression

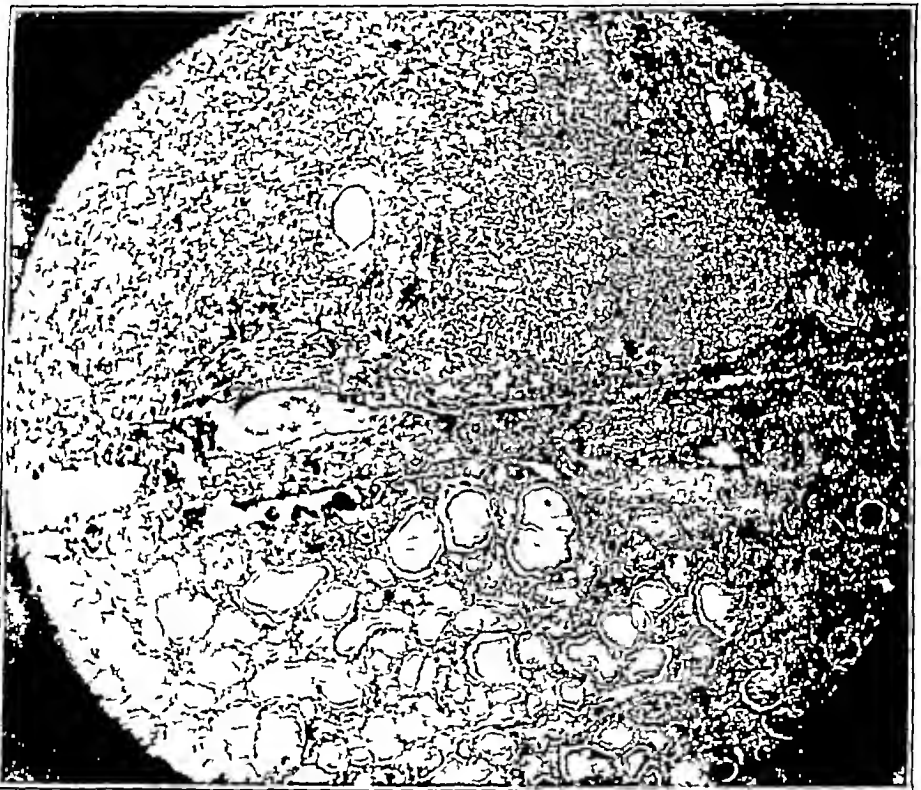


Fig 31—Section also from tumor shown in figure 26. In the upper portion of the section normal thyroid tissue can be seen separated from the localized area of hypertrophy and hyperplasia by a false or apparent capsule. This section was cut in the same manner as in figure 30 but from a different level. In the lower half of the section is shown the hyperplastic acini are more round and smaller than in figure 30 and show less infolding of the epithelium but are just as typical of hypertrophy and hyperplasia as in figure 30. This demonstrates the difference in the appearance of hypertrophy and hyperplasia of the thyroid epithelium that may occur not only in different glands or portions of the same glands but even in the same localized nodule. Reduced from a magnification of  $\times 575$ .

exerted on the connective tissue septums traversing the gland parallel to the chyma of adjacent lobules. Distortion of the contiguous normal thyroid tissue was apparent (figs 20, 21, 23 and 32). In between the

septa, forming the (apparent) capsule, could often be seen small groups or clusters of acini which in the majority of instances were of the normal structure, but which not infrequently presented the histologic appearance of hypertrophy and hyperplasia (figs 22, 23, 26, 29, 30, 31 and 32). Whether these areas were tongue-like diverticula from the main area of hypertrophy and hyperplasia, or whether they were the beginning of another lobule, was not determined. These islands of parenchyma demonstrated the possibility that a capsule might result from compression of the thyroid tissue and stroma surrounding these

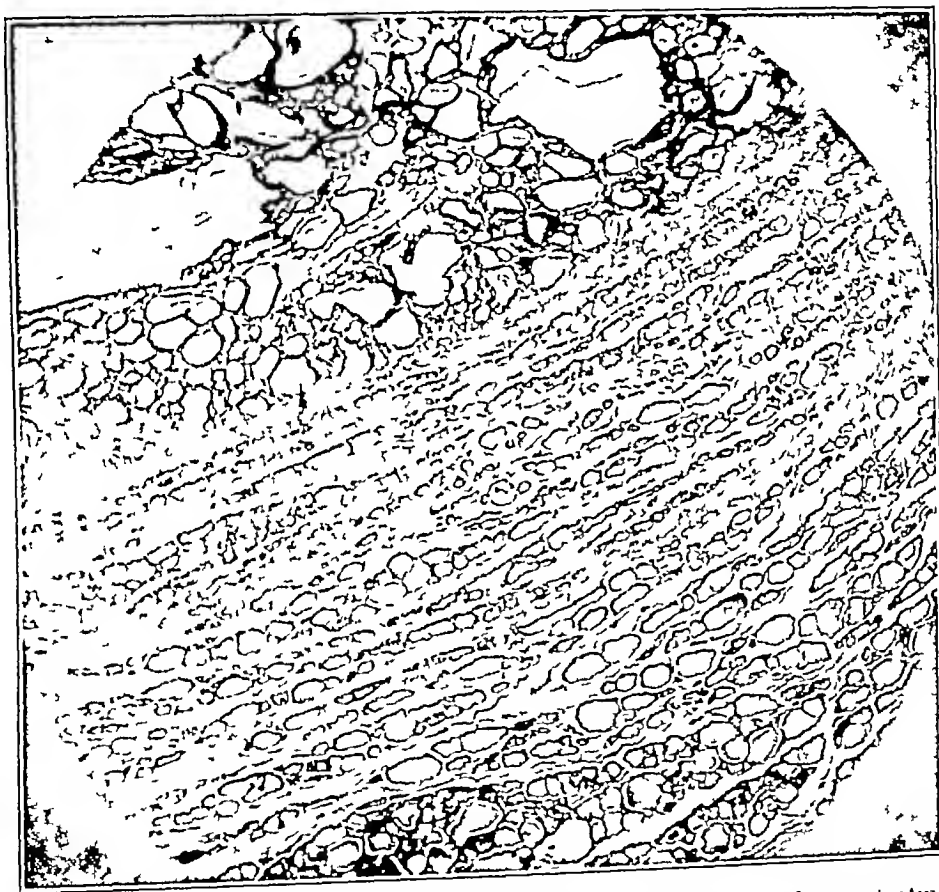


Fig 32—Section from portion of tumor shown in figure 20 demonstrating in the upper portion, the hyperplastic portion of the tumor and the peripheral compression of normal thyroid tissue and the fibrous septums, which is the forerunner of the capsule. Reduced from a magnification of  $\times 57$ .

areas of localized hypertrophy and hyperplasia. As a rule, these areas were further demarcated by a peripheral infiltration of small lymphocytes. Even if after continuing for years, the disease cycle of remissions and exacerbations had run its course, in a localized area or lobule, one would expect to find microscopic evidence of hypertrophy and hyperplasia together with those of involution (figs 27 and 28). The proportion of evidently functioning intact parenchyma to the portion showing histologic regression differed in these localized regions of

On the other hand, since in six of nine cases of true Ménière's disease there is loss of both vestibular and cochlear functions, it seems more reasonable to expect the lesion—in these cases at least—to be primary in the nerve itself rather than in the peripheral end-organs. Given the objective evidence of unilateral deafness without vestibular alteration, there are only two possible sources of the offending lesion, namely, the cochlear nerve or the cochlear end-organ. For practical purposes, the exact location does not matter. Section of the acoustic nerve should produce the same result in either point of origin. It is not improbable that the character and location of the cause may not always be the same.

#### COMPARISON OF MENIERE'S DISEASE WITH TIC DOULOUREUX AND EPILEPSY

In the symptomatic expression of Meniere's disease one is strongly reminded of other human ills, such as trigeminal neuralgia, glossopharyngeal neuralgia, and possibly of epilepsy. In all there is the same periodicity of attacks, coming on without warning and without apparent cause—all suggesting lesions of nerves or of nerve tracts or systems. In cases of neuralgia, the symptoms remain confined to the domain of the affected nerve, but in epilepsy whole systems, i e., those controlling consciousness, motor and sensory function, speech, taste and others, may be and usually are involved by the spread of the stimulus. It has been learned from experiments on animals that any cerebral defect is a potential source of epilepsy, that although the cells of the motor cortex are responsible for the remarkable phenomenon of clonic convulsions, lesions of the connecting fibers even far removed from the motor cortex, may induce attacks of precisely the same general character as when the motor cortex is involved directly. Are not Ménière's attacks in reality like seizures of epilepsy (or of trigeminal or glossopharyngeal neuralgia) differing only in that a different and independent part of the nervous system is affected? In either case any defect in the nerve circuit is always a locus minoris resistentiae removing the inhibition which holds functions under control and permitting their explosion as it were. It may be asked whether such a comparison of Meniere's disease with epilepsy is justified because in the former there is always a progressive objective loss of function (hearing). In cases of epilepsy there may or may not be progressing loss of function, the actual result depending on the character of the underlying cause, but regardless of the kind of lesion the expression of the convulsion is just the same. The same is true of trigeminal or glossopharyngeal neuralgia. The characteristic ticlike pain is precisely the same whether a tumor is the offending cause or whether the cause escapes the present inadequate tests.

It is useless to speculate further concerning the character of the lesion causing Meniere's disease, or its precise location within the limits

## MICROSCOPIC ANATOMY OF THE NERVES THAT LEAD TO THE LUNGS

Numerous investigators have carried out extensive studies on the microscopic course of the nerve fibers to the lungs. Braencker<sup>11</sup> reviewed the work of the various investigators in detail, therefore we shall mention only the conclusions which were reached by their studies. Van Gehuchten and Molhant<sup>12</sup> showed that the bronchomotor fibers of each vagus have their origin in the dorsal nucleus of that nerve, and from that nucleus they extend without interruption to the hilum of each lung. It is still undetermined whether or not these fibers are interrupted in the peripheral ganglions of the lungs, but most investigators agree that it is probable that such an interruption actually takes place. The experimental evidence in favor of this assumption can be found in the report of Mollgaard.<sup>13</sup> He succeeded in completely removing one lung in two young dogs without producing any degeneration of the cells in the dorsal nucleus of either vagus nerve. In these same dogs, he found many degenerated nerve cells in the middle cervical sympathetic ganglion on the side where he had previously performed the pneumectomy. Only a few degenerated cells were found in the middle cervical ganglion of the opposite side. Further studies on the same animals failed to show any direct connection between the nerves to the lungs and the spinal cord. The cells in the stellate ganglions did not show any changes, although a few nerve cells showing marked chromolysis were found in the second and third thoracic sympathetic ganglions.

In similar experiments on cats Mollgaard<sup>14</sup> showed that most of the degenerated nerve cells were found in the stellate ganglions. The middle cervical ganglions are not always present in that animal, but in those animals in which the ganglions were present there was some degeneration of the nerve cells in them following pneumectomy. From the foregoing experiments, we may draw the following conclusions. There are fibers which go directly from the dorsal nucleus of each vagus to the hilum of the corresponding lung where they are interrupted for the first time in the peripheral ganglions of that lung. The middle cervical and stellate ganglions, together with the second and third thoracic sympathetic ganglions, constitute the sympathetic centers of the lungs (fig 5).

*The Possibility of Denervating One Lung*—After a careful consideration of all the data which we have presented on the macroscopic and microscopic course of the nerves leading to the lungs, the ques-

13 Van Gehuchten, A., and Molhant. Contribution a l'etude anatomique du nerf pneumogastrique chez l'homme, Bull Acad roy de Belgique 25 859, 1911.  
14 Mollgaard, H. Studien über das respiratorische Nervensystem bei den Wirbeltieren, Skandin Arch f Physiol 26 315, 1912.

just defined Frankl-Hochwart mentioned leukemia, syphilis, rheumatism and trauma as predisposing causes and reported cases to support this statement. Recently I saw a patient (not included in this report) afflicted with Ménière's disease and with proved syphilis of the nervous system. In none of the nine cases in this report has there been any of the predisposing causes mentioned by Frankl-Hochwart. The uniform absence of a history of otitis media or of mastoid infection, or of a positive Wassermann reaction from the blood is worthy of note.

It would seem that the treatment in cases of true Ménière's disease by section of the eighth nerve has precisely the same rationale as section of the sensory root of the trigeminal or glossopharyngeal nerves in *tic douloureux*. If the attacks begin either in the eighth nerve or in the cochlea—and they begin in one or the other—and if the lesion is strictly unilateral, impulses can no longer be transmitted after section of the nerve. It is then hardly conceivable that future attacks are possible after section of the eighth nerve. Moreover, since section of the nerve is central to the ganglionic cells in the semicircular canals and cochlea, regrowth of the nerve and recurrence of the attacks should be precluded. If these impressions and deductions are correct, section of the eighth nerve should serve as a therapeutic test of Ménière's disease just as section of the trigeminal sensory root or of the glossopharyngeal nerve are tests for *tic douloureux* of these nerves.

#### SUMMARY AND CONCLUSIONS

1 Intracranial section of the affected eighth nerve is suggested as a cure for Ménière's disease. This operation has been performed on nine patients, none of whom has had a subsequent attack. The elapsed time since operation varies from three months to three and one-half years.

2 The operation should be attended by no mortality and with no after-effects, since the patients are practically deaf in the affected ear before operation.

3 Although the series of cases is small, the results suggest that section of the acoustic nerve should stop Ménière's attacks just as absolutely as intracranial section of the glossopharyngeal nerve or of the sensory root of the trigeminus stops the attacks of *tic douloureux* in these two nerves.

4 The symptoms and signs of Ménière's disease are analyzed. The dizziness of Ménière's and pseudo-Ménière's diseases are compared with that of other known lesions—tumors, inflammations and aneurysms—in the cerebellum and brain stem.

5 There appear to be reasons to doubt that the cause of Ménière's disease is primary in the semicircular canals. A primary lesion of the acoustic nerve seems a more probable primary source of the attacks.

tion arises as to the possibility of completely denervating the lungs of an animal for experimental purposes. Our studies have been made on dogs because the innervation of the lungs in that animal is the most constant, and also because of the accurate data on the anatomy and physiology of the nerves to the lungs that is available

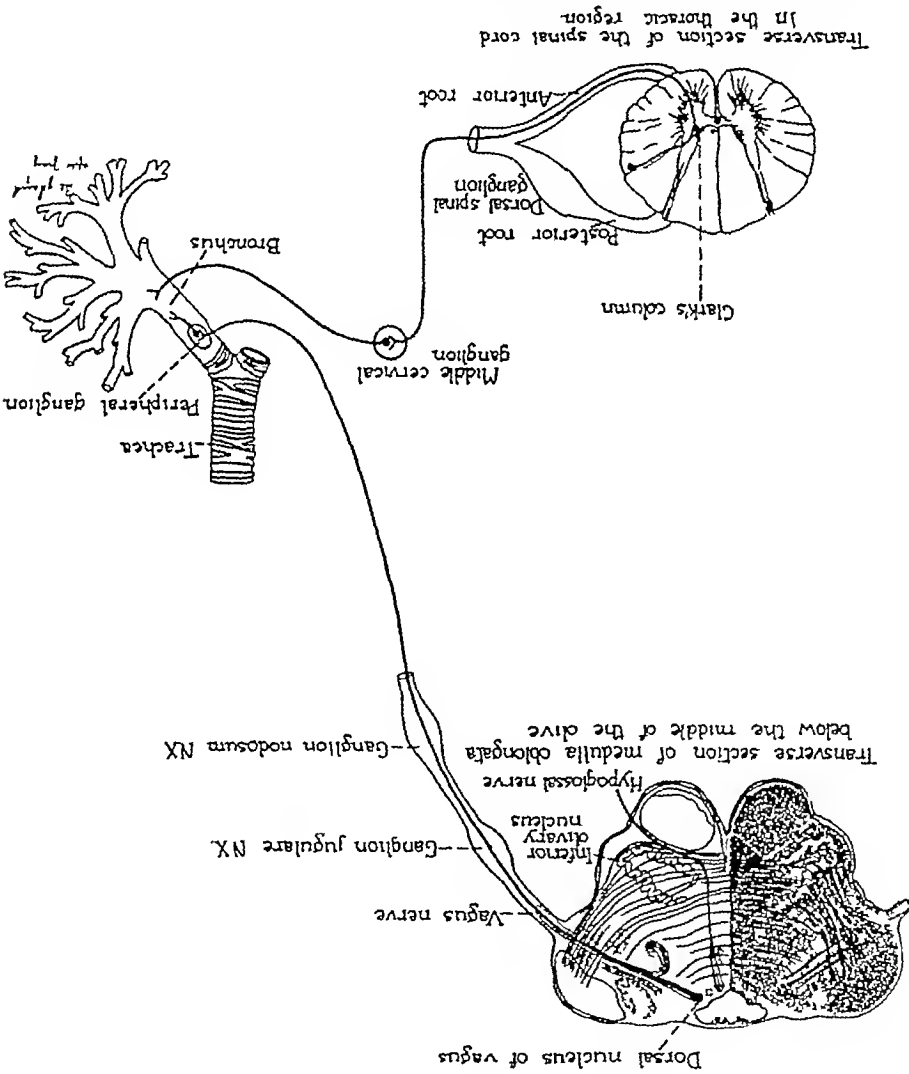


Fig 5—Diagram showing the course of the efferent sympathetic nerve fibers to the lung from the nuclei in the medulla oblongata by way of the vagus nerve, and from the nuclei of Clark's column in the spinal cord by way of the thoracic ramus communicans

From the theoretical standpoint, the lungs can be denervated by two different methods. The first method consists of the removal of all the sympathetic branches to the lung, as well as the removal of a section of the vagus nerve on the same side. The second method consists of the removal of the fibers from the peripheral plexuses at a point just before they enter the hilum of the lung

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The sympathetic fibers to the lungs come from the spinal cord by way of the superior thoracic ram communicantes. The fibers then enter the stellate ganglion and pass through the ansa Vieussens into the middle cervical ganglions. From there they reach the lungs through the anastomoses which these ganglions have with the recurrent laryngeal and the inferior tracheal nerves, the aortic plexus and the inferior cardiac nerves. Consequently, below the ganglions the pulmonary fibers of the sympathetic trunk are much scattered, and it is difficult to isolate and identify them during any surgical procedure. These fibers are confined to definitely recognizable nerves only in the region of the ganglions, and it is in this region that they should be severed during the operative procedure. Similar results can be accomplished by cutting the ram communicantes of the last cervical and the first seven thoracic sympathetic ganglions. The method of multiple ramisection described by von Gasa<sup>12</sup> would make this procedure an easy one, but, as we have shown, the ramisection would not eliminate the fibers from the various ganglions. Mollgaard<sup>11</sup> showed by his experiments that these ganglions are important centers, and that they are able to function even after they have been completely separated from their central connections. Consequently, we believe that it would be necessary to remove completely the middle cervical ganglion, the stellate ganglion, and the second, third, and fourth thoracic sympathetic ganglions in order to interrupt the direct pathway of the nerves to the lung. In the dog, however, the middle cervical ganglions are usually within the common vagosympathetic trunks, therefore, in order to remove them completely, it is necessary to remove a section from each of the vagosympathetic trunks. It is only in rare cases that the middle cervical ganglions can be separated from the common vagosympathetic trunks. From the experimental standpoint, this fusion of the middle cervical ganglions with their corresponding vagosympathetic trunk is important, since the removal of that ganglion necessitates the removal of a section of the vagus nerve on that side and consequently removes that vagus as a source of nerve supply of the lungs. On each side just above the middle cervical ganglion the recurrent laryngeal nerve becomes separated from the vagus. Thus, by removing a section of the common vagosympathetic trunk for a distance of 1 cm on either side of the middle cervical ganglion, we simultaneously interrupt the two main nervous pathways to that lung.

From our study of these nerves, we conclude that in order to eliminate simultaneously and as completely as possible the vagus and

12 V Gasa, W. Die Resektion der paravertebralen Nerven und die isolierte Durchschneidung des Ramus communicans, Arch f klin Chir 133 479, 1924, Klin Wchnschr 25 525 1924

# EXPERIMENTAL STUDIES ON DENERVATED LUNGS\*

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There is no vital structure in the body that is so frequently the seat of disease as the lung, still the practical importance of the innervation of this organ is not generally appreciated. The complexity and often the contradictory evidence regarding this innervation have prevented the real facts from being disseminated even in medical schools. Recent evidence, however, emphasizes the important rôle which the nerves that lead to the lung may play in clinical disorders. Binger and his associates<sup>1</sup> have shown that the tachypnea which accompanies acute pulmonary disease in the absence of anoxemia is of nervous origin. The cause of sudden death in cases of pulmonary embolism and following thoracentesis, as well as the cause of bronchial asthma and allied conditions, may also be nervous in origin. It has also been suggested that postoperative massive atelectasis (collapse) of the lungs may, in part, be due to a disturbed innervation. Our interest in this matter arose from the hope that following experimental alterations in the nerves that lead to the lungs we might be able to reproduce the latter condition. Our studies deal with the possibility of complete denervation of the lungs, the methods used to produce partial denervation of one lung and the changes in the physiology of respiration that were produced by such denervation. Before entering into the details of this study, it seems wise to outline briefly the anatomy and the histology of the nerves to the lungs.

## MACROSCOPIC ANATOMY OF THE NERVES TO THE LUNGS

In man, the bronchi and the lungs receive their innervation from the plexuses of nerves which surround the bronchi in the region of the hilum of each lung (fig 1). These plexuses are made up of fibers from the vagal nerves and the cervical sympathetic trunk of the corresponding side, schematically, they may be divided into two main plexuses called the anterior and the posterior pulmonary plexuses. It

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<sup>1</sup> Binger, C A, Boyd, D, and Moore, R L. The Effect of Multiple Emboli of the Capillaries and Arterioles of One Lung, *J Exper Med* **45** 643, 1927.

the sympathetic part of the innervation of one lung, it is necessary to resect the first four thoracic sympathetic ganglia to remove the ansa Vieusseni and the stellate ganglion, and to resect that portion of the vagosympathetic trunk which has included in it the middle cervical ganglion. All this should be done on the side on which the denervation is to be accomplished.

METHODS FOR SECTIONING THE EXTRINSIC NERVES OF ONE LUNG

The sectioning of the extrinsic nerves of one lung may be done either by the cervical or by the intrathoracic approach.

*The Cervical Approach*—In several dogs we succeeded in removing the stellate ganglion by using a cervical approach which was similar to the one outlined by Professor Leriche<sup>16</sup> for the extirpation of that ganglion in man. The approach was made through a low cervical incision just behind the anterior border of the sternocleidomastoid muscle. The stellate ganglion lies immediately beneath the vertebral artery and can be readily exposed by a slight anterior retraction of that artery. From this incision, it is also possible to remove without much difficulty that section of the vagosympathetic trunk which has included in it the middle cervical ganglion. The cervical approach, however, makes the resection of the third and fourth thoracic sympathetic ganglia practically impossible. As we have shown, these thoracic ganglia have numerous important connections with the nerves that lead to the lungs, consequently, those pathways must be interrupted if we hope to produce the denervation of one lung. It is because of this difficulty that we have used the transthoracic route in our studies on dogs.

*The Transthoracic Approach*—In man, the thoracic sympathetic ganglia and trunks can readily be reached by an extrapleural approach similar to the operation proposed by Torek<sup>17</sup> for the exposure of the thoracic part of the esophagus. In dogs, however, the extrapleural route would necessitate a long and difficult operation. In our experience, the transthoracic approach is well tolerated by the dogs and it overcomes many of the technical difficulties that are encountered in the other procedures.

#### TECHNIC OF OPERATION

The dog is first completely anesthetized by the drop ether method and then a large soft rubber catheter is inserted into the trachea and artificial respiration is instituted by means of the Ljungström insufflation apparatus. The amount of

16 Leriche R. De la découverte du ganglion sternal des opérations qui se pratiquent au cœur humain, Lyon Chir. 23 763, 1926.  
17 Torek Franz. The Operative Treatment of Carcinoma of the Esophagus, Ann Surg 61 385 1915. Carcinoma of the Thoracic Portion of the Esophagus, Arch Surg 10 353 (Jan) 1925.

has been shown that there is a rich anastomosis between the fibers of the plexuses on the same side as well as between the fibers from the corresponding group on the opposite side

*The Branches of the Vagi that Lead to the Lungs*—The majority of the fibers from the vagi come from the intrathoracic portion of that nerve, while only a few come from the inferior cardiac and

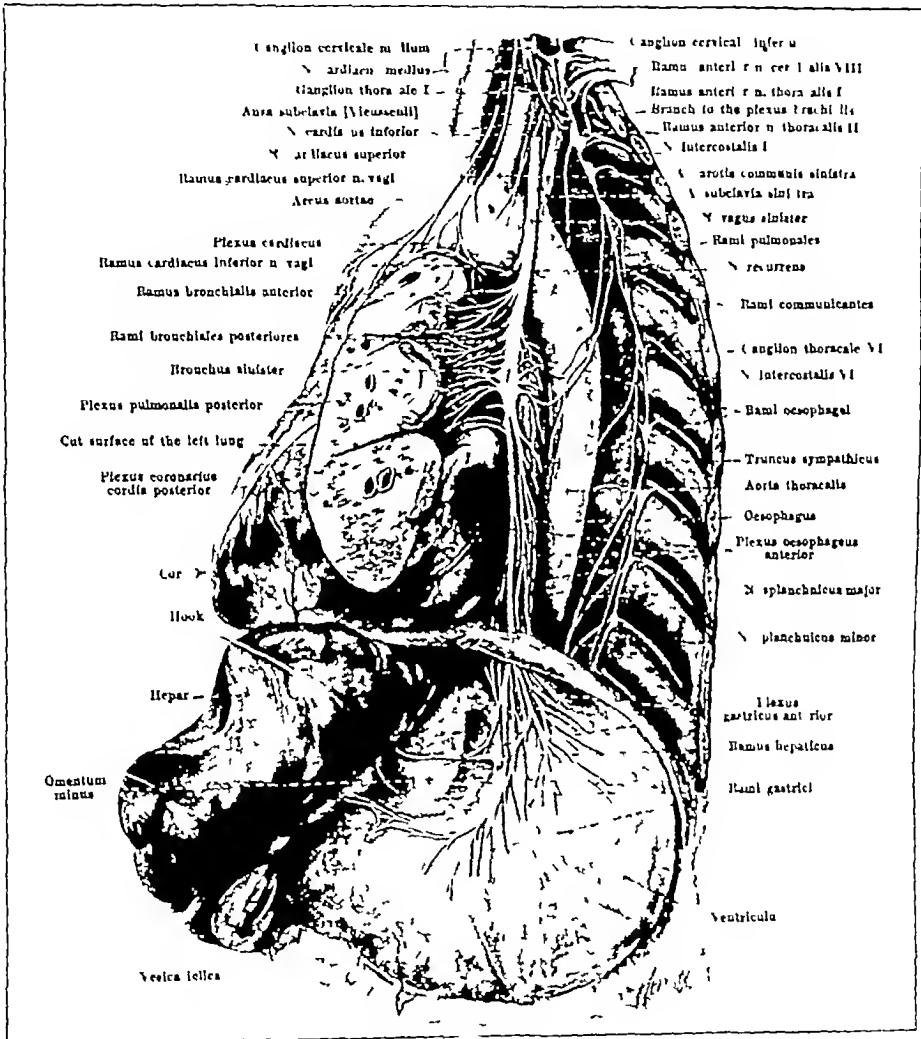


Fig 1—The course and branches of the left vagus nerve in the thoracic and abdominal cavities of man (from Spalteholz Atlas, ed 4)

recurrent laryngeal nerves. The branches from the latter nerves, however, vary greatly in number and in size. From a gross anatomic standpoint, the fibers from the vagal nerves are much more numerous than those from the sympathetic trunks. Hovelacque,<sup>2</sup> in his recent

2 Hovelacque, A. Anatomie des nerfs craniens et rachidiens et du système grand sympathique chez l'homme, Paris, Doin, 1927, vol 1, p 232

ether vapor in the system is regulated so that the animal is kept well anesthetized during the entire operation. The dog is then placed on its right side, and the operative field is thoroughly cleansed with alcohol and 1:5,000 mercuric chloride solution. After the sterile linen draping has been applied, an incision about 10 cm in length is made in the second intercostal space. The incision is carried to the parietal pleura, after which the bleeding vessels are carefully clamped and tied with silk. The parietal pleura is then incised, and the upper lobe of the left lung is retracted to obtain a good exposure in the region of the angle of the second rib. The sympathetic trunk is then visible through the posterior parietal pleura. This pleural covering is incised, and the sympathetic trunk is dissected out to a point well below the fourth thoracic sympathetic ganglion (fig 6). All the rami of the upper four thoracic ganglia, as well as the rami

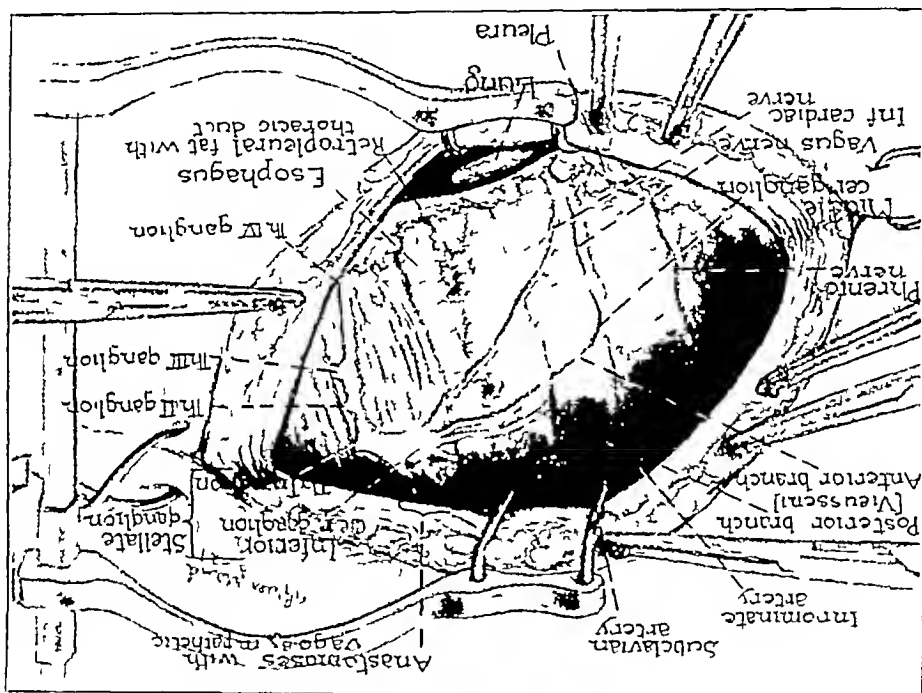


Fig 6—Exposure of the stellate ganglion and its branches by the trans-thoracic route

of the stellate ganglion are isolated. The excision is begun from below, the sympathetic trunk below the fourth thoracic ganglion being severed first. After all the branches of the fourth, third and second thoracic ganglia have been severed, the lateral branches of the stellate ganglion are isolated and severed. The stellate ganglion is dissected out and the anterior and posterior branches of the ansa Vieusseni are identified and freed. The posterior branch is cut and the anterior branch is followed to its junction with the middle cervical ganglion in the common vagosympathetic trunk (fig 7). The portion of the vagosympathetic trunk which has included in it the middle cervical ganglion as well as the origin of the recurrent laryngeal nerve is then completely resected. Hemorrhage during this procedure is practically negligible. Two fine silk sutures are used to approximate the edges of the posterior parietal pleura at the site of the operation. The anterior parietal pleura is closed by

book, stated that each vagus sends the following branches to the lungs and bronchi

1 The tracheal branches which form a plexus that surrounds the trachea and both primary bronchi

2 The anterior pulmonary branches which arise from a small branch of each vagus in its intrathoracic suprabronchial course. The end branches of these nerves enter the hilum of the lungs on the anterior side of the pulmonary vessels. Taft<sup>3</sup> stated that frequently the anterior pulmonary branches arise from the middle, but more constantly from the inferior cardiac nerves

3 The bronchopulmonary nerves consist of from four to six branches from the main trunk of each vagus. The branches unite to form the anterior and the posterior pulmonary plexuses. Some of these fibers enter the bronchial wall immediately, but the majority follow the posterior wall of the primary bronchi and enter the hilum of the corresponding lung. At this point some of the fibers leave the bronchial wall and course between the visceral pleura and the pulmonary parenchyma for a considerable distance. Other branches from the same plexuses follow the course of the pulmonary veins, and according to Cruveilhier,<sup>4</sup> frequently a small branch is found on the posterior side of the pulmonary arteries

*The Sympathetic Branches that Lead to the Lungs*—There is a rich anastomosis between the sympathetic fibers and the fibers from the vagi so that many of the sympathetic fibers also enter into the formation of the pulmonary plexuses. In general, however, the majority of the sympathetic fibers come from the inferior cervical ganglions and from the first four thoracic sympathetic ganglions. In addition, there are a few fibers from the cardiac nerves which go to the lungs by way of the bronchi and a still smaller group of fibers that accompanies the bronchial arteries

*The Peripheral Ganglions*—In 1840, Remak<sup>5</sup> described the numerous separate ganglions which are interlaced between the fibers that make up the pulmonary plexuses. Later Schiff,<sup>6</sup> Kolliker,<sup>7</sup> Toldt,<sup>8</sup> and Kandarazki<sup>9</sup> showed that these ganglions vary greatly in size and in number, but they are always numerous along the bronchi near the hilum

3 Taft, cited by Hovelacque (footnote 2)

4 Cruveilhier, cited by Hovelacque (footnote 2)

5 Remak, R., *Ztschr. d. Verhandl. f. Heilk.*, 1840

6 Schiff, *Arch. f. Physiol. Heilk.* 6 792, 1853

7 Kolliker, *Arch. f. mikr. Anat.* 2 320, 1854

8 Toldt, Carl, *Lehrbuch der Gewebelehre mit vorzugsweiser Berücksichtigung des menschlichen Körpers*, ed. 3, Stuttgart, 1888

9 Kandarazki, M., *Ueber die Nerven der Respirationswege*, *Arch. f. Anat. u. Entwicklungsgesch.* 1 11, 1881

a continuous fine silk suture. The intercostal muscles are closed with interrupted chromic catgut sutures. Just before the second row of interrupted sutures are tied, a hemostat is inserted between the ribs into the pleural cavity. The hemostat is used to spread the soft tissues, and the lungs are inflated to expel the air from the pleural cavity. The subcutaneous tissues are brought together by interrupted silk sutures, and the edges of the skin are approximated in a similar manner.

If peripulmonary sympathectomy is to be performed at the same time as the foregoing procedure, it is better to make the incision in the third intercostal space, since this approach gives a better exposure of the pulmonary artery and

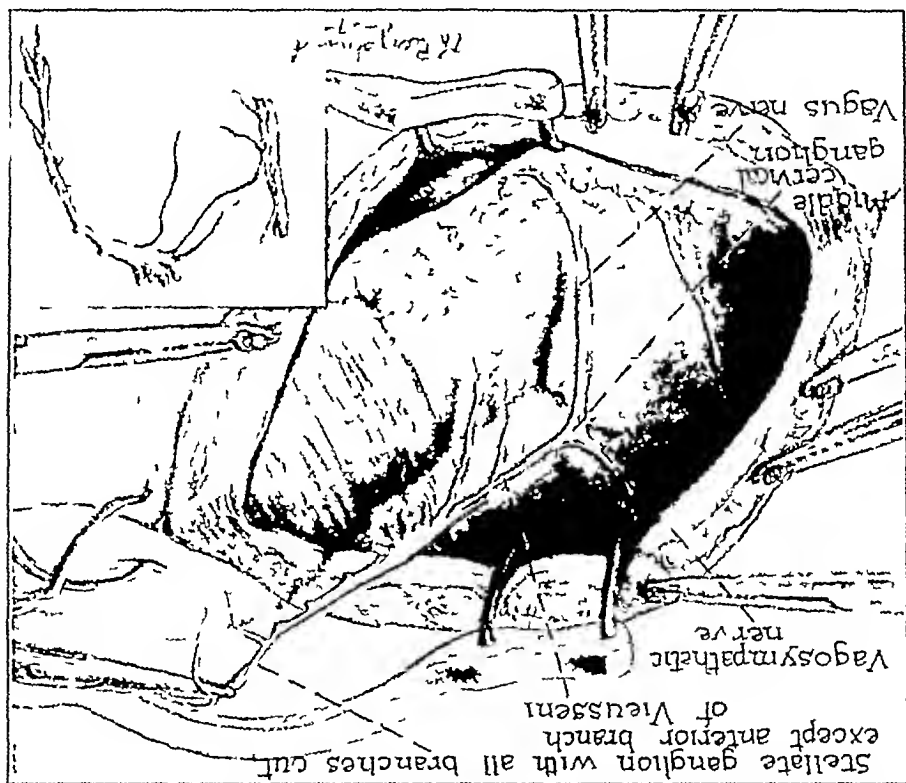


Fig 7—Method of resecting the stellate ganglion and its branches. The anterior branch of the ansa Vieussens is used as a guide to the middle cervical ganglion which is included in the common vagosympathetic trunk.

does not make the resection of the stellate ganglion and its branches any more difficult. We have used the latter procedure on three dogs with satisfactory results.

*Comments on the Operative Procedures*—The question arises as to the possibility of producing a complete denervation of one lung. It one recalls the macroscopic and microscopic studies of the nerves that lead to the lungs, one sees that even after such extensive operations as we have already described there are still two sources of nervous impulses that have not been interrupted. The first source is from the ganglions that are situated within the bronchial walls, while the

of each lung. They also showed that some of these ganglions are situated in the superficial layers of the tracheal and bronchial walls, while others are deeply embedded in the submucosa. Izmajloff<sup>10</sup> also described a fine network of nervous fibers in the submucosa of the bronchi which are in direct connection with these ganglions.

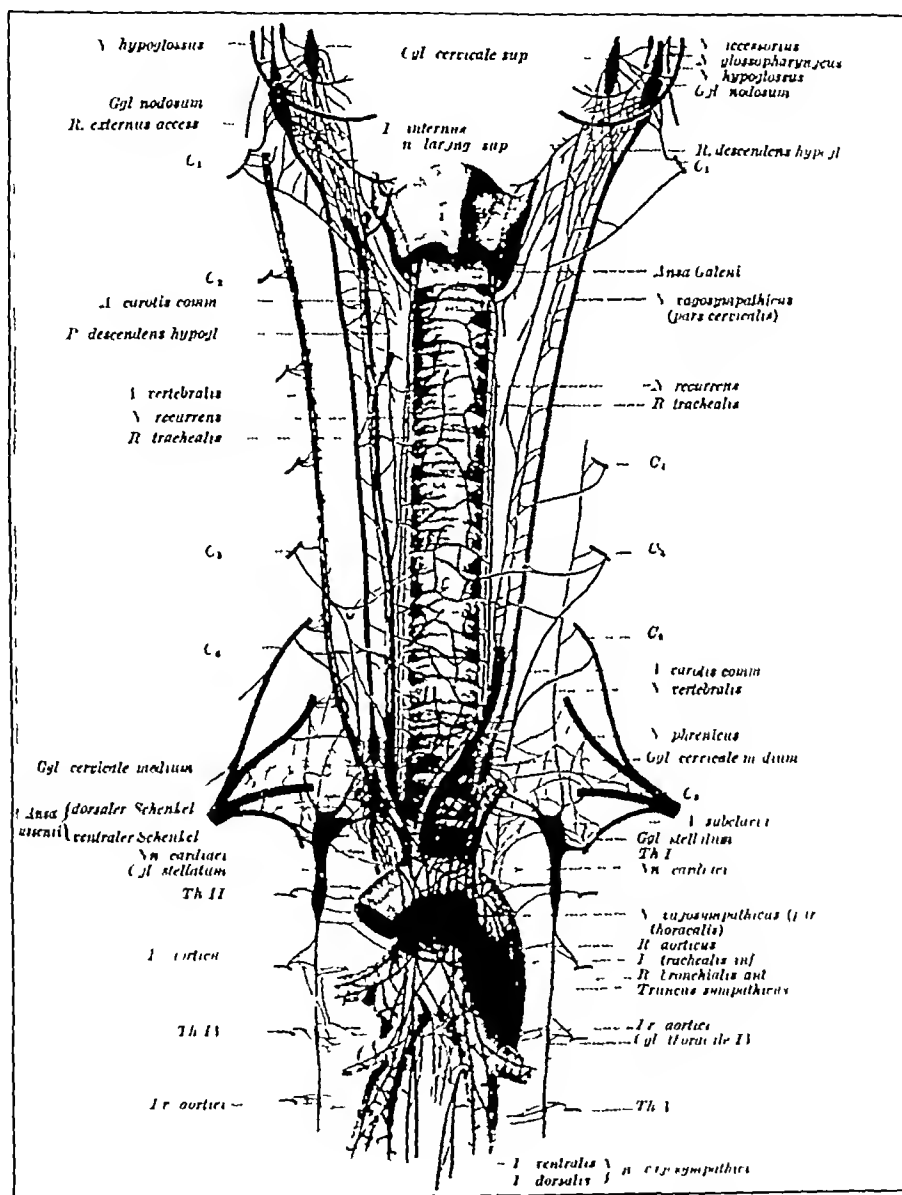


Fig 2—Anterior view of the nerves from the tracheobronchial trunks in the dog (from Braeucker<sup>11</sup>)

From the work of the foregoing investigators, it is evident that there is a marked difference between the innervation of the lungs in

<sup>10</sup> Izmajloff. Zur Histologie der Nerven in den Atmungsorganen, Thesis, St. Petersburg, Jahresb. f. Anat. u. Physiol., 1873, p. 157.



other source is by way of the fine anastomotic fibers from the pulmonary plexuses of the opposite side. Hence, we must conclude that this surgical procedure does not produce a complete denervation of one lung when the procedure is performed on only one side. In the studies which we were interested in making, it was necessary to keep the nerve supply of one lung intact in order that the reaction of the partially denervated lung could be compared with its normal mate. For this reason, bilateral extirpation of the nerve trunks to the lungs was not used in any of the experiments which we report here. However, even after bilateral extirpation of these nerves there would still be one source of nervous impulses to the lungs, namely, the peripheral ganglia that are situated in the walls of the trachea and bronchi.

Theoretically, it is possible to produce a complete denervation of one lung by removing all the fibers that make up the peripheral pulmonary plexuses on one side. These plexuses, as we have shown, contain all the sympathetic and vagal fibers for one lung. Technically, this is an extremely difficult procedure, since the fibers are so numerous and some of them are so fine that we can never be certain that all the fibers have been interrupted. We have attempted this procedure on several dogs, but after killing the animals and carefully examining the site which had previously been occupied by the pulmonary plexuses, we invariably found several fibers that had not been severed during the operation. We have also tried to denervate one lung by bronchial denudation, but this procedure is likewise an uncertain one in regard to complete interruption of all the nervous pathways to that lung.

#### RESULTS OF THE STUDIES ON DOGS IN WHICH THE EXTRINSIC NERVES OF ONE LUNG HAD BEEN SEVERED AT OPERATION

A series of ten dogs in which the extrinsic nerves to one lung had been severed was used for these studies. The dogs were observed over periods varying from several weeks to several months and the data which we obtained may be grouped under the following five headings: *Effect on the Respiratory Movements*—The frequency and character of the respiratory movements were charted for several days prior to the operation, and a normal respiratory curve for that animal was plotted. For several weeks following the operation a similar record was kept. In analyzing the various curves, it was found that there was no constant change in the respiratory movements after the extrinsic nerves to one lung had been severed. Likewise, the rate or volume of the pulse following the operation was not altered, the immediate postoperative reaction which usually lasted for a few hours is excluded.

man and in the various experimental animals, yet when we consider all animals in one group we find that there is more variation in the fibers from the sympathetic trunks than there is in the fibers from the vagi. It has been only within recent years that the exact anatomy of the nerves leading to the lungs of the various experimental animals has been worked out. Braeucker<sup>11</sup> added much information to this subject by his work on dogs.

In the dog the nerve supply of the lungs is likewise derived from the vagi and from the cervical sympathetic trunks (figs 2 and 3). The fibers from the vagi reach the lung by two main routes, namely,

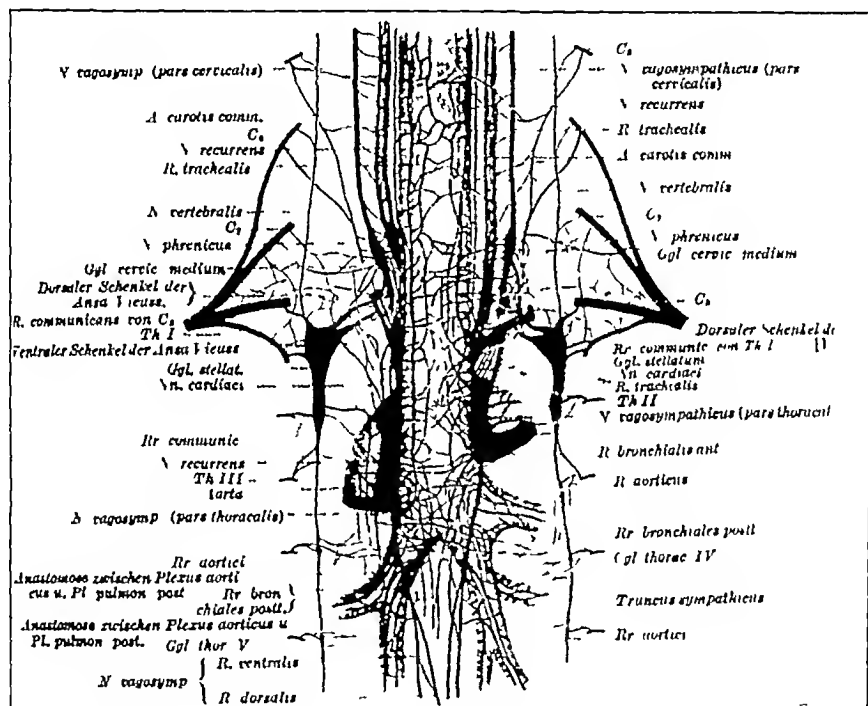


Fig 3—Posterior view of the nerves from the tracheobronchial trunks in the dog (from Braeucker<sup>11</sup>)

by the anterior bronchial nerves and by the posterior pulmonary nerves. The former are branches of the inferior tracheal nerves which come from the vagi through the recurrent laryngeal nerves. The posterior pulmonary nerves consist of from four to nine distinct fibers. Three of these fibers are usually well developed and arise from each vagus at the inferior border of the primary bronchus. The branches of the nerves surround the major bronchus and form the posterior pulmonary plexuses. Scattered between the nerve fibers are

<sup>11</sup> Braeucker, W. Die experimentelle Erzeugung des Bronchialasthmas und seine operative Beseitigung, Arch. f. klin. chir. **137**: 463, 1925, *ibid.* **139**: 1, 1926.

*Effect on the Carbon Dioxide Combining Power of the Blood Plasma.*—These determinations were made according to the method of Van Slyke and Neil<sup>18</sup>. From the table it is evident that there was not a constant variation in the results following the operation. The slight diminution which followed immediately after the operation usually returned to normal within two days. In some of the dogs, there was a slight increase which persisted over a period of several weeks, but this increase was so slight that it never exceeded the limits of normal variation. The table illustrates the average variation in three different animals as well as the reaction which follows the operation.

*Effect of Various Kinds of Experiment Fimbriae.*—In this series of experiments, we compared the reaction of a partially denervated lung with that of its normal mate after various kinds of experimental control had been injected into the general circulation by way of the external

*Reactions in the Carbon Dioxide Combining Power of the Blood Plasma Before and After Partial Denervation of the Lung*

Dog Was		Dog Was		Dog Was		Dog Was		Dog Was		Dog Was	
Date	Blood (cc)	Date	Blood (cc)	Date	Blood (cc)	Date	Blood (cc)	Date	Blood (cc)	Date	Blood (cc)
May 28	10.11	Preoperative fimbriae for control				July 2	17.7	Dog Was			
May 11	15.10	Postoperative fimbriae				July 11	11.14	Dog Was			
June 1	12.19	June 17				15.28	Dog Was				
June 1	12.82	June 21				15.10	Dog Was				
June 7	5.11	July 7				15.17	Dog Was				
July 7	11.10	July 7				15.27	Dog Was				

\* For blood, combined at 0 (control) and 20 mm. pressure

In several of the dogs of this series, we injected (1 cc) of a thick suspension of hyaloprotein in a saline solution into the jugular vein. One month after the original injection, the same procedure was repeated and the dog was killed three days later. Similar experiments were performed with a mucopolysaccharide suspension of potato starch in saline solution. The general results were the same in both groups of experiments. At autopsy numerous small yellow spots were found in the lungs. Microscopically, the small yellow areas were shown to be small abscesses. There was no difference between the abscesses in the partially denervated lung in comparison with those in the lung which the nerve supply remained intact (fig. 9).

*Effect on the Gross and Microscopic Anatomy of the Lung.*—The lungs of various kinds of animals after the section of the external nerves

<sup>18</sup> Van Slyke, E. D. and Neil, J. M. quoted by Michael, J. R. *Physiology and Biochemistry in Modern Medicine* ed. J. St. Louis, C. V. Mosby 1922, p. 12, J Biol Chem 61 514, 1924

numerous ganglions of various sizes. The anastomosis with the fibers from the opposite side takes place largely by way of the inferior tracheal nerves. The majority of the sympathetic fibers reach the lung by an indirect route. Some of the sympathetic fibers are distributed to the lungs through the subclavicular plexuses. These plexuses are made up of fibers from the middle cervical<sup>12</sup> and stellate ganglions, from the posterior branch of the ansa Vieusseni and from the rami communicantes of the seventh cervical and the first thoracic ganglions.

Other sympathetic fibers go to the lungs by way of the recurrent laryngeal and the inferior tracheal nerves. Part of these fibers come directly from the middle cervical ganglions, and part of them course through the inferior cardiac nerves. The fibers from the recurrent laryngeal, the inferior tracheal and the inferior cardiac nerves are all grouped together to form the anterior pulmonary plexus, particularly on the right side. The inferior cardiac nerve on that side is made up of two branches from the right vagosympathetic trunk, one branch from the recurrent laryngeal nerve, one from the anterior loop of the ansa Vieusseni, one from the left middle cervical ganglion, one from the left recurrent laryngeal nerve, and one from the left vagosympathetic trunk. All these nerves have a rich anastomosis with both stellate ganglions and the upper thoracic rami communicantes of both sides.

On the left side, the aortic plexus sends numerous fibers to the pulmonary plexuses. The aortic plexus is made up of fine branches from the upper thoracic rami communicantes of both sides (fig. 4).

In the dog, the general distribution of the peripheral ganglions in the walls of the trachea and the bronchi is essentially the same as we have already described for man, consequently, we shall omit the repetition.

In general, there are two groups of nerves which contribute to the innervation of the lungs. The first group consists of fibers from the vagi which course through the bronchopulmonary and the recurrent

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<sup>12</sup> Braeucker,<sup>11</sup> in his work on the dog, has shown that the ganglion which is included in the common vagosympathetic trunk is in reality the middle cervical ganglion and should always be referred to by that name. Many other investigators, however, refer to that ganglion as the inferior cervical ganglion. We agree with Braeucker that the ganglion which receives the last cervical ramus communicans should be called the inferior cervical ganglion, and the ganglion which receives the first thoracic ramus communicans should be called the first thoracic sympathetic ganglion. In man as well as in the dog, the real inferior cervical ganglion is usually fused with the first thoracic ganglion and it is this association that should be called the stellate ganglion. For this reason the middle ganglion should always be called the middle cervical ganglion, in spite of the fact that it sometimes lies deep in the thorax, even as low as the second rib.

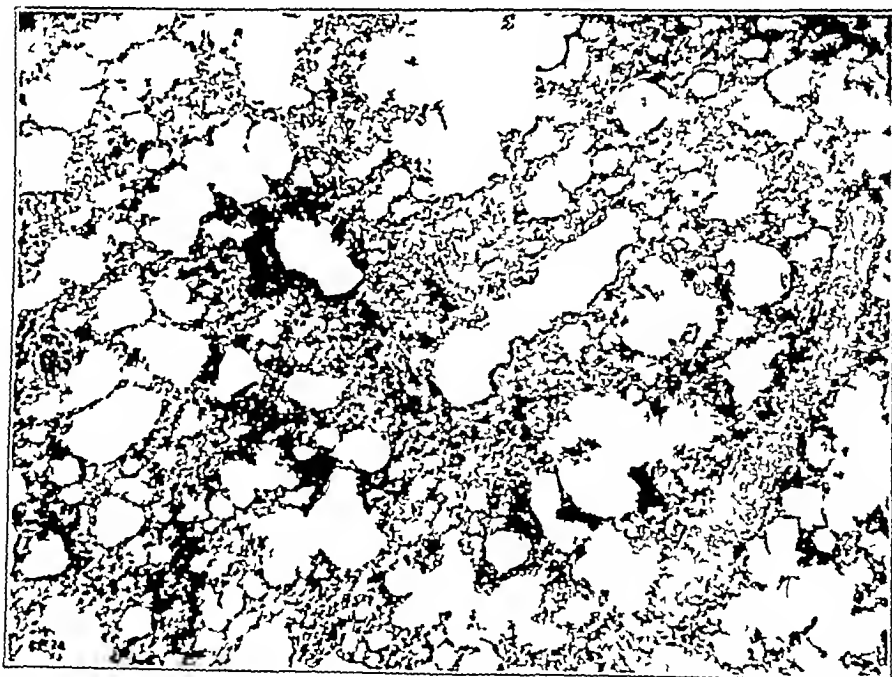


Fig 8—Photomicrograph of a section taken from the right lung of a dog in which a suspension of lycopodium and acacia had been injected into the left jugular vein three days previously. Numerous small abscesses were present throughout the entire lung,  $\times 100$

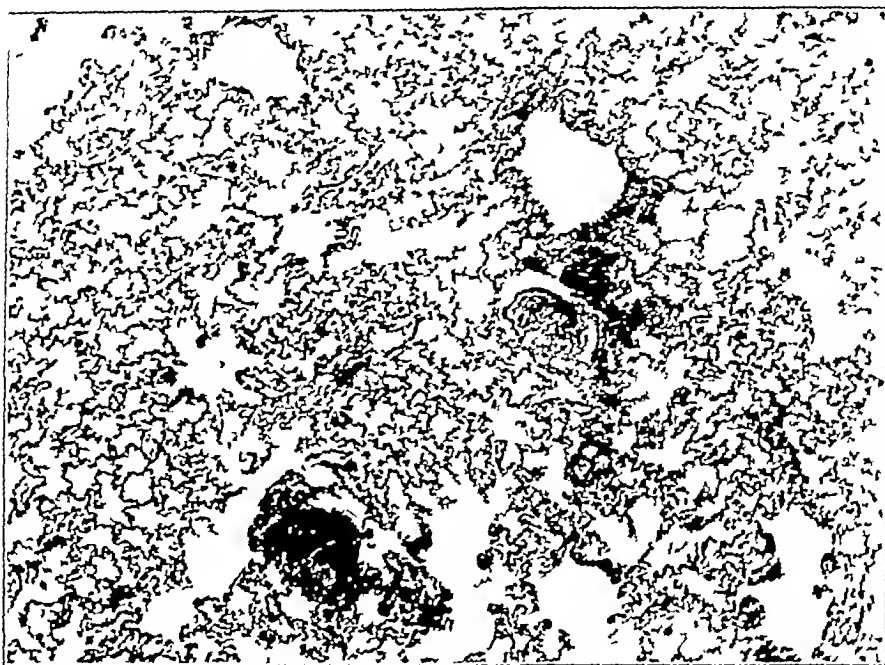


Fig 9—Section from the upper lobe of the partially degenerated left lung of the same animal as figure 8, showing similar small abscesses,  $\times 100$

laryngeal nerves The other group of fibers comes from the middle cervical and the stellate ganglions of the sympathetic trunks by way of the inferior cardiac nerves and by way of the ansa Vieusseni There are also several small branches which go directly from the thoracic ganglions to the lungs along the course of the bronchial arteries In the dog, the bronchopulmonary innervation comes from two major plexuses, namely, the anterior pulmonary plexuses and the

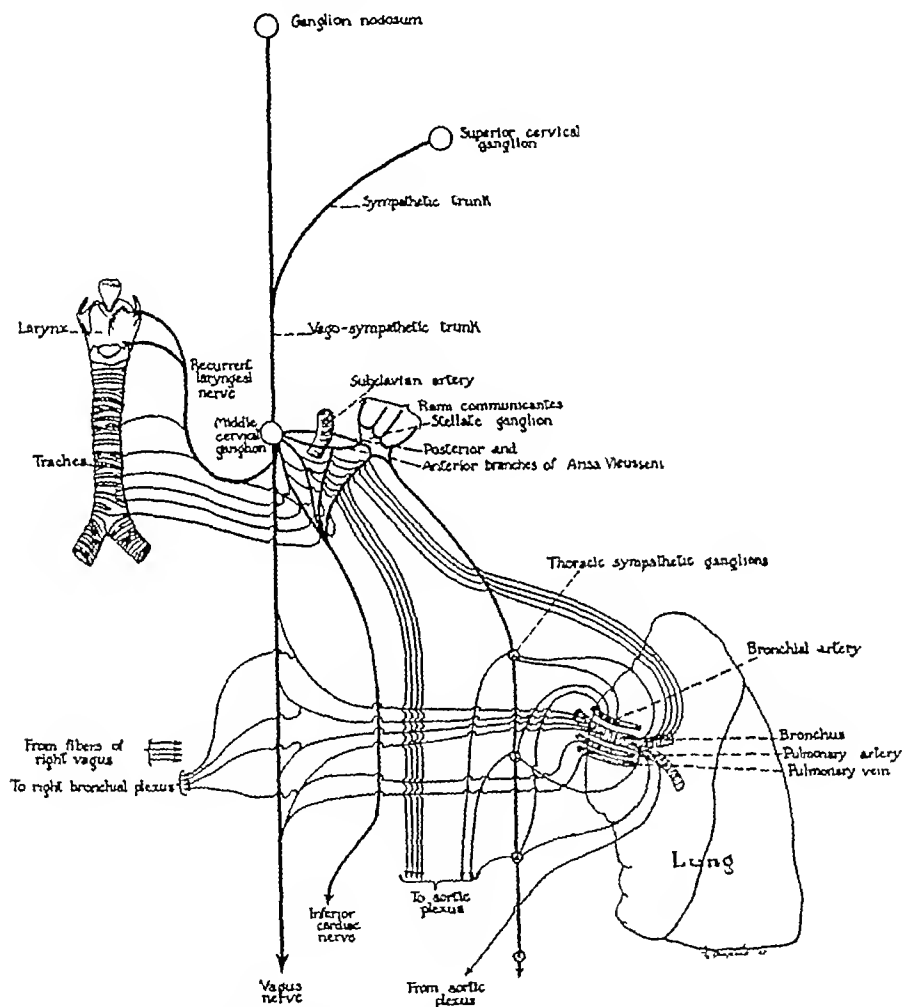


Fig 4—Diagram showing the origin of the various sympathetic nerve fibers which go to the left lung of the dog

posterior pulmonary plexuses The former are made up of branches from the inferior cardiac nerves together with the inferior tracheal branches of the vagus nerves The posterior pulmonary plexuses contain only fibers from the vagi There is a rich anastomosis, however, between the two plexuses as well as between these plexuses and the tracheal and pulmonary plexuses of the opposite side On the left side, the anterior pulmonary plexus receives fibers directly from the aortic plexus (fig 4)

to one of the lungs did not show any evidence of changes from the normal. In two of the dogs a few adhesions were found between the lung and the healed operative wound. In none of the dogs were we able to find any evidence of congestion, edema or other pathologic change.

#### *Massive Atelectasis (Collapse) in a Partially Degenerated Lung—*

One of our dogs developed a typical massive atelectasis (collapse) of the lungs three days after we had severed the extrinsic nerves to the left lung. The immediate postoperative course of this dog was entirely normal. Studies of the carbon dioxide combining power of the blood plasma both before and after the operation did not show any variation from the normal. The frequency and character of the respirations prior to the occurrence of the massive atelectasis were normal. There was no evidence of inflammation about the operative wound. The dog had been active and apparently had not suffered any ill effects from the operation. The animal was placed on the operating table for the purpose of obtaining a specimen of blood for the estimation of the carbon dioxide combining power of the plasma. The dog was quickly turned on its back and immediately became deeply cyanotic, respirations ceased within a short time, and finally the heart ceased beating. A roentgenogram of the chest taken at this time showed the diaphragm on the left side to be higher than it had been on the previous control roentgenograms. Displacement of the mediastinum was not demonstrable in the roentgenograms.

Autopsy revealed a typical massive atelectasis (collapse) of the entire left lung and a partial atelectasis of the lower lobe on the right side. The operative wound was entirely healed. The upper part of the right lung appeared normal. Free fluid was not found in the pleural cavities. In the dog, the mediastinal membrane which separates the two pleural cavities has been shown by Alatas<sup>19</sup> and others to be delicate, it is, therefore, fair to assume that when an acute condition such as massive atelectasis occurs on one side, the physical signs which characterize this condition in man may not occur, if the mediastinal membrane ruptures before the heart can be drawn to the affected side. The rupture of this interpleural membrane may explain the difference between the clinical picture of massive atelectasis (collapse) of the lung in man and in the dog.

Macroscopically, all the major and minor bronchi were dissected out but evidence of obstruction could not be found. The bronchi were normal in appearance and contained practically no secretion. One of the lobes of the collapsed lung was remsufflated, and the pulmonary

<sup>19</sup> Alatas, Rudolph. So-called Mediastinal Septum of Dog in Relation to Pneumothorax Problem in Man. Arch Surg, 8:336 (Jan.) 1924.

In the younger patients the evidence of histologic regression was less pronounced, and almost the entire nodule was composed of tissue of the normal structure of the thyroid which had undergone hypertrophy and hyperplasia. In the older patients with cases of long standing there was a more marked degree of histologic regression, so that the nodules although much larger about the size of a lemon, were composed almost entirely of fibrous tissue, extra-acinar colloid from disintegrated acini and a few scattered acini still remaining intact, surrounded by a small peripheral rim of hypertrophic parenchyma (figs 27 and 28). This condition in the older patients was probably due to the greater frequency of the completion of the morbid cycles and the consequent gradual reduction of the parenchyma due to the process of involution that accompanied each remission. Thus, it is conceivable that if a sufficient number of the disease cycles were completed, there would eventually be an entire loss of function in that region in which substitution of the parenchyma by fibrous tissue had occurred (figs 25, 27 and 28).

The parenchyma intervening between these localized areas of hypertrophy and hyperplasia was normal thyroid tissue in all respects (figs 19, 20, 22, 23, 24, 29, 30, 31 and 32). As it was evident (1) that the patients had a clinically apparent hyperthyroidism (2) that this was associated with a goiter in which the nodular elements were composed of localized areas of thyroid parenchyma presenting the characteristics of histologic appearance which has come to be recognized as those of hypertrophy and hyperplasia, together with those regressive disintegrating changes that must now be recognized as being characteristic of involution, (3) that the intervening parenchyma was normal in all respects, it would seem justifiable to conclude that these localized areas or nodules were the cause of the symptoms of hyperthyroidism in these cases. To this must be added the fact that when these areas or nodules were shelled out or removed by resection of the lobes of the gland the clinical state of hyperthyroidism disappeared. The histologic alterations associated with the hypertrophy, hyperplasia and involution or in other words, with the disease cycle of hyperthyroidism demonstrated to occur throughout the thyroid as a whole in exophthalmic goiter were thus found to be present even when the disease process was confined to a few or more sharply localized areas of the gland while the normal structure of the hyperplastic thyroid parenchyma was maintained, and there was no evidence of the formation of new tissue or the histologic structure of the thyroid gland. Both of these facts speak against the likelihood of these areas being of a purely focal nature, whereas the histologic appearance would suggest that they are isolated regions or lobules of hyperfunctioning parenchyma. The disease cycle hypertrophy and hyperplasia occurred many times



## COMMENT

In a recent review of all the cases of hyperthyroidism in the Johns Hopkins Hospital, of which there were 710, together with 200 cases from three other hospitals in Baltimore, The Church Home and Infirmary, The Union Memorial Hospital and The Woman's Hospital, hypertrophy and hyperplasia of the parenchyma of the thyroid gland were demonstrated in every case. Hence, it can be stated definitely that, so far as our experience goes, the clinical syndrome, hyperthyroidism, has always been associated with hypertrophy and hyperplasia of the parenchyma of the thyroid. Moreover, it was thought that the microscopic appearance of the glands in these cases corresponded, as a rule, to the degree of hyperthyroidism—the more severe the clinical syndrome, the greater was the amount and extent of the hypertrophy and hyperplasia and vice versa. In 100 of these cases in which the clinical course had been acute and fulminating and in which neither artificial nor spontaneous remissions had occurred, there were found on microscopic examination a diffuse hypertrophy and hyperplasia of the thyroid, but no evidence of involutional changes. In seven cases in which the thyroid was examined before, during and following an artificial remission associated with iodine treatment, it was demonstrated that involutional changes occurred diffusely throughout the gland as a whole, but that in certain regions these had exceeded the average amount and had progressed to the formation of microscopic and even clinically palpable nodules which presented the histologic evidence of regression and even of disintegration. These areas or nodules were termed involutional bodies or areas of hyperinvolution and occurred in 200 cases of exophthalmic goiter in which the patients had undergone artificial remissions as a result of treatment with iodine. In fifty cases of severe hyperthyroidism—typical exophthalmic goiter—in which several spontaneous remissions had occurred, the thyroid was nodular and irregular in shape, and the patients gave the history of the nodules appearing in the gland during a remission following one of the exacerbations. On histologic examination, these nodules were composed of tissue similar in all respects to the involutional bodies or areas of histologic regression noted as developing during an artificial remission caused by iodine, and were involved in the present exacerbation just as was the remainder of the parenchyma of the gland as a whole. It is, therefore, possible for hyperthyroidism associated with a smooth diffuse hypertrophy and hyperplasia of the thyroid to give rise to a nodular gland or goiter as a result of artificial or spontaneous remissions with an associated involution of the gland. Thus, in cases of nodular goiter associated with hyperthyroidism in which the nodules showed the exact microscopic structure and appearance of these involutional bodies and in which the characteristic histologic changes—hypertrophy and hyper-

tissue immediately appeared normal (fig 10) Microscopic sections from the affected lung showed the histologic picture of complete atelectasis (figs 11, 12, 13, 14 and 15) Careful search of even the smallest bronchi did not reveal evidence of obstruction or of abnormal accumulation of secretion The alveolar walls were completely collapsed, and cellular infiltration could not be demonstrated (fig 15)

#### COMMENT

In the foregoing case, the massive atelectasis (collapse) of the lung was not due to bronchial obstruction It is interesting to note that section of the extrinsic nerves to that lung did not prevent the occur-

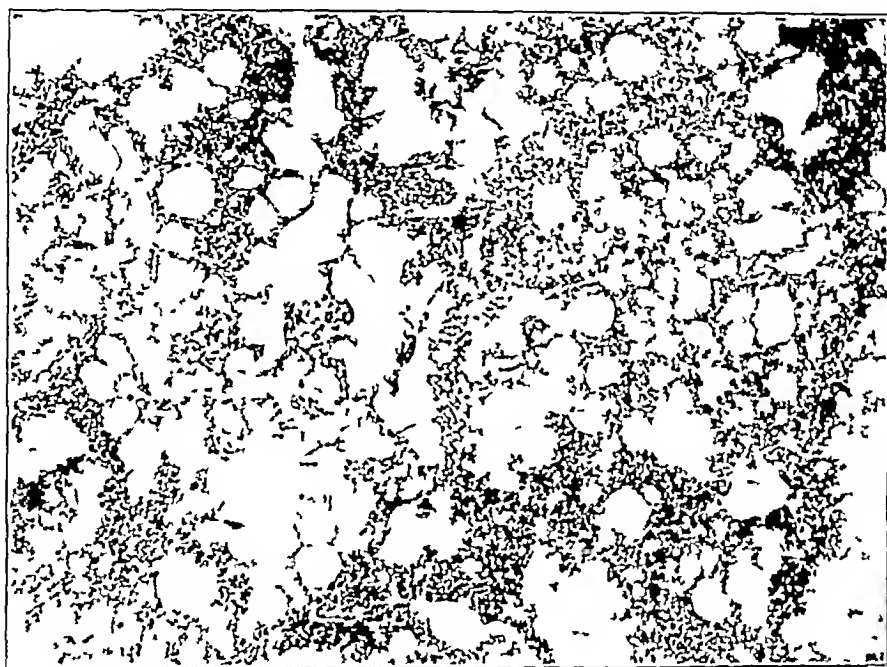


Fig 10—Section from the upper lobe of the collapsed left lung after it had been remsufflated,  $\times 100$

rence of the massive atelectasis (collapse) If there was any reflex responsible for this collapse, the impulses must have come by way of the anastomotic branches from the opposite side, or they must have originated in the peripheral ganglions of the affected lung It would be interesting to know if after a bilateral section of the extrinsic nerves to the lungs, massive atelectasis (collapse) of either lung could occur So far we have not been able to produce massive atelectasis (collapse) at will, therefore, further studies along this line cannot be made at this time

In our series we were unable to show any constant change in the frequency or character of the respiratory movements Papillian and

Our knowledge of the exact causation, development and character of the lesion known as osteochondritis dissecans is not exact, nor fully explanatory. Since Koenig's original observation, little of importance has been added

#### GROSS DESCRIPTION

The articular surfaces of the joint, as a whole, are normal, except for the loose fragment of the internal condyle and slight, irregular linear depressions of the cartilage of the external condyle, which are exaggerated in appearance in the photographs (figs 3 and 4). There is no lifting of the articular cartilage of tibia, femur and patella, nor any pannus formation



Fig 3—A gross specimen from a case of osteochondritis dissecans, the loose body is resting in its bed

The loose fragment is attached on its external border to the posterior crucial ligament by a thin band of fibrous tissue. The articular surface of the fragment is roughly a rectangle with rounded corners, 2 cm in width (internal to the external edge) and 2.5 cm in length (antero-posterior or sagittal plane). The fragment has a maximum thickness of 8 mm, including the articular cartilage which is from 3 to 4 mm thick. A prominent feature of the fragment is a transverse depression, shown clearly in figure 2, which divides it into two halves of about equal size. Beneath the cartilage, the fragment when sawn through shows the subchondral bone separated into two parts by loosely textured fibrous tissue. This is shown clearly in the photomicrograph which is

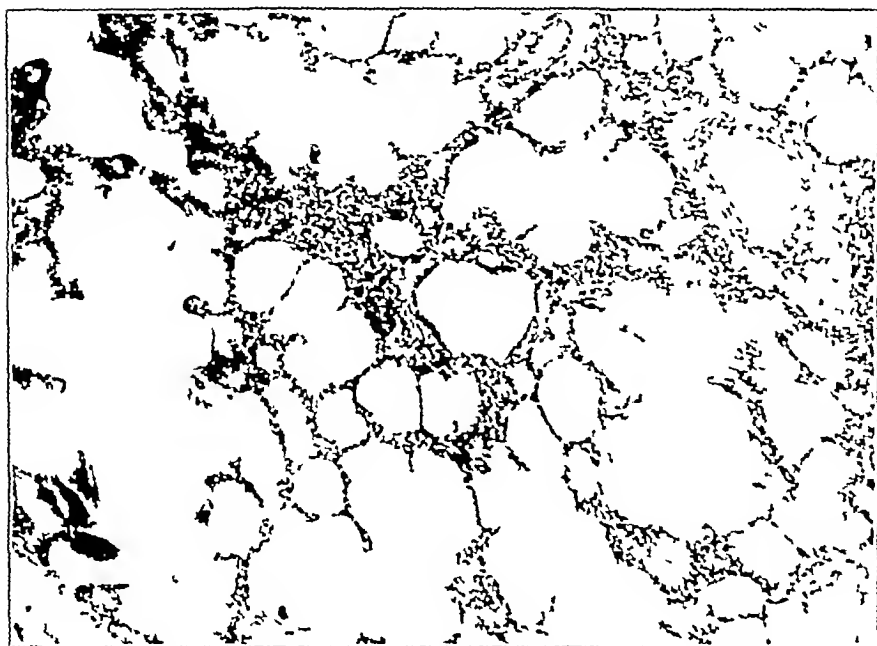


Fig 11—Section from the apex of the left lung of another dog, taken during the operation for partial denervation of that lung. Subsequently this dog developed massive atelectasis (collapse) of this lung. Compare with figure 12,  $\times 100$ .



Fig 12—Photomicrograph of a section removed at autopsy from the right lower lobe after collapse of the lungs had occurred. Note the collapsed alveoli adjacent to a patent bronchus. This section is from the same animal from which the biopsy shown in figure 11 was taken three days previously.  $\times 100$ .

almost a replica of a figure in an article by Axhausen.<sup>1</sup> One cannot escape the conclusion that this buckling was purely a mechanical effect permitted by the character of the tissues deep to the fragment.

On the internal and the external margins, there is a granular cartilage deposit extending for a distance of from 1 to 4 mm on the deep surface of the fragment, continuous with the articular cartilage of the superficial surface. The reparative growth is not present on the anterior and posterior borders of the fragment.

The depression in the femur is smooth and lined with a thin layer of fibrous material. From both lateral margins there is a thin layer of cartilage extending from the surface downward for a distance of



Fig. 4—Same as in figure 3—The loose body is lifted from its bed, and the fibrous attachment to the margins of the internal condyle is shown.

from 3 to 5 mm. On the surface of the condyle at the internal margin of the depression, the articular cartilage shows some fragmentation and separation from the contiguous articular cartilages.

In order to obtain material for microscopic study, a saw cut was made through the internal condyle, passing through the center of the fragment and its socket roughly in the sagittal plane, but at a sufficient angle to avoid continuing the cut into the shaft of the femur. The plane of the section made an angle of 20 degrees with the axis of the shaft of the femur. This cut revealed an irregular cast filled with soft-textured fibrous tissue lying immediately beneath the articular

Cruceanu,<sup>20</sup> however, stated that after section of the sympathetic trunk on one side, the respiratory rate is diminished for a period of about ten days following the operation. The explanation for this change is still lacking, but, whatever the cause may be, there is no doubt that the animal overcomes the effect. Within a few weeks after the operation, change cannot be detected, and the partially denervated lung reacts as its normal mate to all forms of physiologic and pathologic stimulation.

The heart and the intestine likewise cannot be denervated by section of their extrinsic nerves. Leriche and Fontaine<sup>21</sup> have shown that even the blood vessels have their own intrinsic nervous system. Our studies tend to show that the same condition exists in the lungs, and we are



Fig 13—Section from the upper lobe of the left lung of the same animal. There is also a patent bronchus surrounded by completely collapsed alveoli,  $\times 100$ .

convinced that the intrinsic nervous system of the lungs is able to function independently of the central connections. It is highly probable that all organs of the human body likewise have their intrinsic nervous systems and, under the proper conditions, could be made to function even after they had been separated from their central connections.

20 Papillian, V., and Cruceanu, H. Der Einfluss den beider Cerv Sympath auf die Respirationsbewegungen, *Clujul Med* 4 1, 1923.

21 Leriche, R., and Fontaine, R. Faits chirurgicaux pour servir a la critique des theories actuelles de la vasomotricite. *Presse med* 31 481 1927. *Recherches experimentales sur l'innervation vasomotrice, le reflexes vasculaires des membres*, *ibid.* 51 852 1927.

depression. In fact, it was separated from it only by 2 or 3 mm of cancellous bone. It measured roughly 1.5 by 2.5 cm, and was irregular in outline. At a plane slightly external to this, as revealed in the sectioning of the slab removed for histologic purposes, there was another small cyst which shows well in figure 5.

#### MICROSCOPIC DESCRIPTION

The crater was lined with a thin layer of poorly-staining, refractive fibrillary material, containing few cells. Its structure indicated that it was probably atypical connective tissue. There was complete absence



Fig 5—Osteochondritis dissecans, low power photomicrograph of a section removed from the specimen which cut through the loose body and the femoral condyle. In this section, the cysts in the condyle lying below the level of the loose body crater are clearly shown. The buckling of the articular cartilage on the surface of the loose body is evident. Reduced from a magnification of  $\times 19$  diameters.

of bone repair such as would accompany a fracture or an experimental incision of the bone in animals. The bone trabeculae of the crater wall, where they were in contact with the lining membrane, were thin and irregular, having the appearance of being excavated on their superior surfaces. There was a zone of deeply granular material between the bone and lining membrane, and the impression was that the bone matrix had undergone

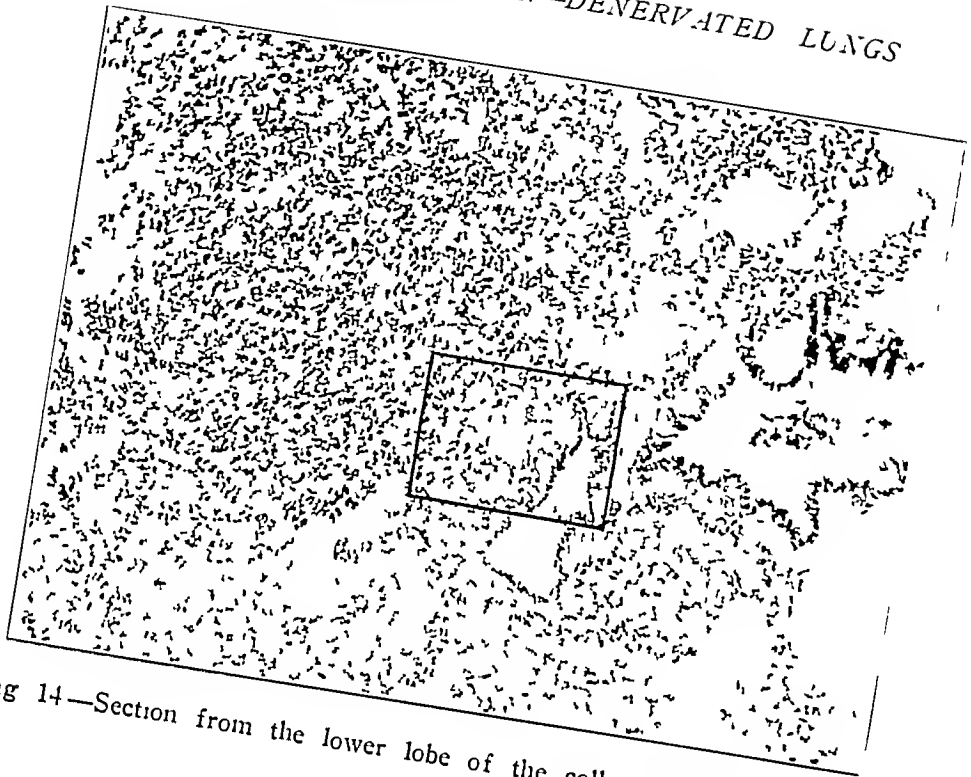


Fig 14—Section from the lower lobe of the collapsed left lung,  $\times 100$

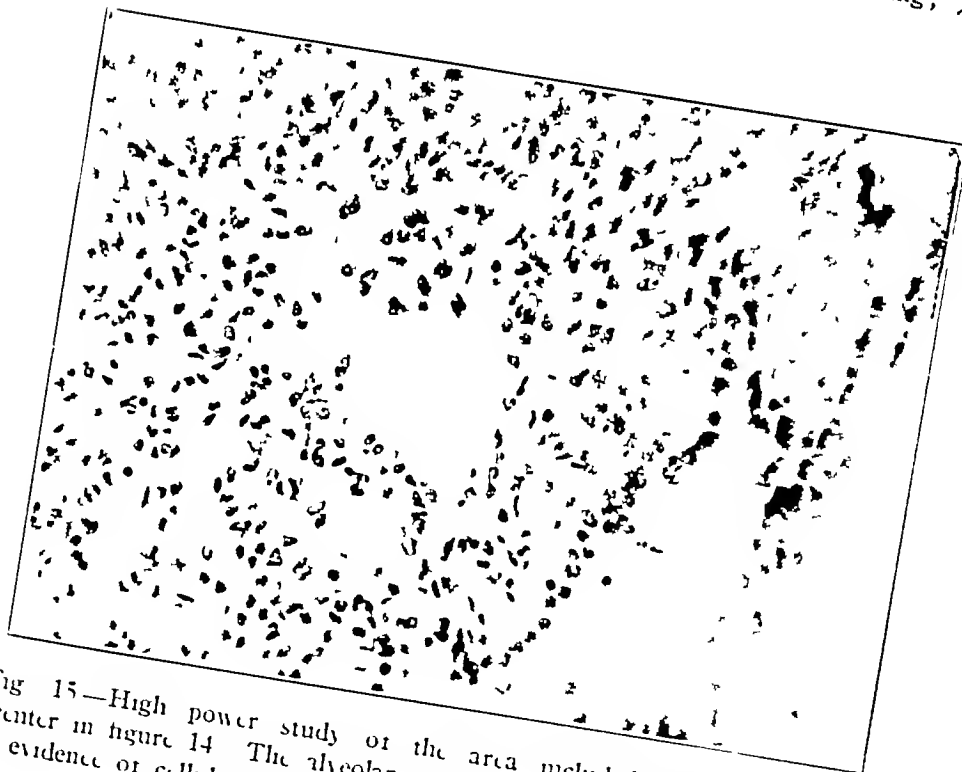


Fig 15—High power study of the area included in the square near the center in figure 14. The alveolar walls are completely collapsed and there is no evidence of cellular infiltration  $\times 430$



autolysis and released its mineral content. Cartilage cells were present here and there throughout in the crater wall close to the bone. Near the periphery or rim of the crater, they formed a thin, definite layer of cartilage with columns of cartilage cells and continuous with the articular cartilage. Thus the impression was forced on us that we were dealing with an unfamiliar reparative process without blood vessel formation, in which cartilage cells apparently originated from bone corpuscles released from the underlying trabeculae.

The cartilage of the fragment appeared to be viable. The cells were normal in appearance. The matrix stained less densely than normally, and this fact, together with the increased thickness of the layer of cartilage as a whole, is probably best interpreted as due to imbibition of liquid. The cancellous bone of the fragment was wholly dead. The interstices were filled with basic staining, granular detritus. The bone trabeculae were deeply stained with eosin, and were refractive and without stainable cells. Giant cells or other viable cells were not present.

The "cysts" may be described as regions devoid of bone trabeculae and without specialized boundary zones. The bulk of tissue in these regions was a loose-textured, myxomatous-like connective tissue enclosing small numbers of fat cells. In places, there were dense fibrous tissue bands traversing these regions. At the peripheries there were compact fibrous tissue or merely the normal fat laden cells of the marrow. In many regions, fat cells were separated by faintly staining material containing delicate fibrin strands, migrating polymorphonuclear leukocytes and mononuclear cells—acute changes explained by the presence of blood vessels filled with chains of streptococci, the evidence of a terminal septicemia.

Blood vessels were numerous in these "cysts," except in central regions in which the tissue was compact. Here there were few blood vessels and large extents of tissue had none. Small circular, outlined cavities were found in such regions, the result of necrosis and liquefaction, as shown by the fact that the immediately adjacent fat and loose-textured fibrous tissues were without nuclei and presented other evidences of death. In many places throughout the "cysts" the impression was obtained that the fat cells had undergone necrosis, without decomposition of the fat, and that the myxomatous appearance of the intervening connective tissue was a consequence thereof, and to be interpreted as edema with a vascular organization.

Important lesions of arteries and veins were absent throughout the extent of the cancellous bone.

As is obvious from the foregoing account the histologic observations have not yielded any clue to the processes antecedent to the separation of the fragments. Neither is there any explanation of the origin of the cysts.

Our experiments tend to throw some light on the explanation for the numerous failures which follow operations on the sympathetic or parasympathetic systems in the surgical treatment of bronchial asthma. We exclude, of course, the failures due to improper diagnosis and improperly performed operations, since these causes for failure have been considered in detail by Leriche and Fontaine<sup>22</sup>. The failures of relief after such operations are still numerous, even in typical cases of asthma in which no special sensitization for foreign matter can be demonstrated. This must be explained on the basis that the reflex paths to the lungs are not completely interrupted. Theoretically, in order to do this it would be necessary to sever both vagi, to remove both stellate ganglions and to cut the upper four thoracic rami communicantes on both sides. Practically, however, this is impossible in man, since one vagus nerve must always remain intact.

Kummel<sup>23</sup> first proposed the resection of the cervicothoracic sympathetic trunk for relief from bronchial asthma. Subsequently, he modified this procedure by using the intrathoracic approach and severing part of the branches of the pulmonary plexuses<sup>24</sup>.

Our studies have shown that such a procedure is no better than the simple removal of the stellate ganglion. When we consider that the intrathoracic approach is much more dangerous than the cervical approach, we cannot believe that Kummel's second procedure has any advantages over his original one. If, in spite of the added risk, one prefers the intrathoracic route, the operation should consist in the removal of the upper part of the thoracic sympathetic trunk, complete extirpation of the stellate ganglion and, finally, section of the vagus nerve on the same side. We believe, however, that a small number of failures will probably always occur after any of the foregoing procedures in fact even after complete bilateral resection of the extrinsic nerves to the lungs, if that operation could be performed with safety, because of the persistence of the peripheral ganglions situated in the walls of the bronchi. These ganglions probably play an important part in the production of bronchial asthma.

#### CONCLUSIONS

1. In the dog, partial denervation of one lung is a safe surgical procedure and can be accomplished by unilateral resection of the first four thoracic sympathetic ganglions, the removal of the ansa Vieusseni

22 Leriche, R., and Fontaine, R. Sur le traitement chirurgical de l'asthme bronchique, Bull et mem Soc nat de Chir de Paris **52** 748, 1926

23 Kummel, Herman, Sr. Ursache der Misserfolge bei operativer Behandlung des Bronchialasthmas und ihre Beseitigung, Arch f klin Chir **142** 499, 1926

24 Kummel, Herman, Sr. Der heutige Stand der chirurgischen Behandlung des Asthma bronchiale, Therap d Gegenw **68** 15 1927

A return to the study of gross relationships of fragment and cavity encounters two facts for consideration the buckling of the fragment also clearly illustrated by Axhausen, and the discrepancy in size of the fragment and the capacity of the cavity. The buckling of the fragment naturally suggests the effects of the yielding of a surface inadequately supported from below. The presence of the "cysts" or areas devoid of bone trabeculae beneath the cartilage naturally suggests the existence of the requisite mechanical factors before the event. Inspection of the curvature of the articular cartilage in the plane of sections utilized for figure 5 seemed to indicate too great a convexity of the surfaces on each side of the cavity. Therefore, a normal femur was obtained, sectioned in the same place, and superimposed, with the

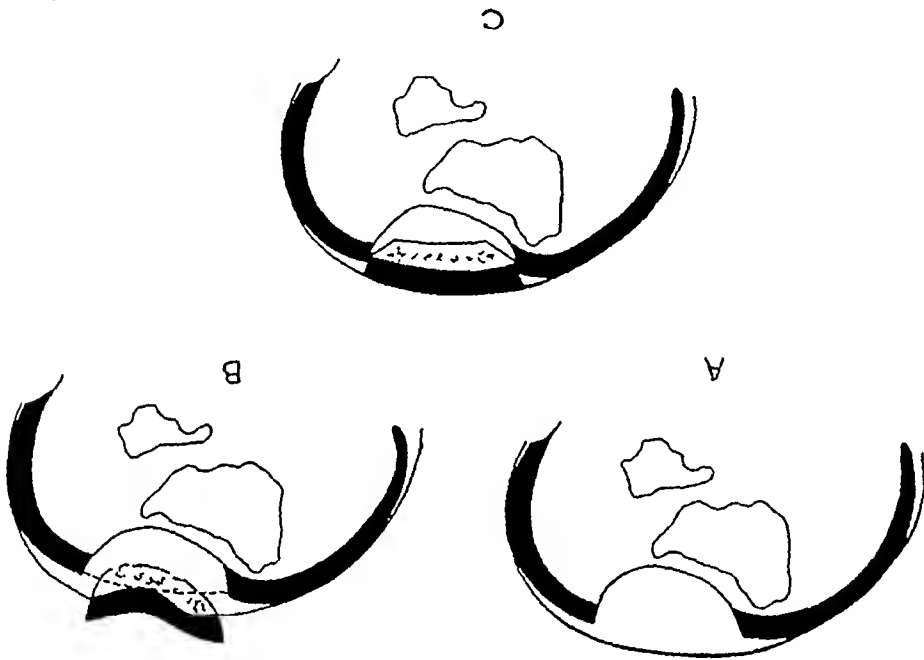


Fig. 6—Osteochondritis dissecans, comparison of the specimen with the outlines of a normal femur which are superimposed. The probable thickness and curvature of the articular cartilage prior to separation of the loose body is shown in *B*. In *C*, the fragment or loose body is represented as restored to its original contour, revealing an unfilled space which existed before the separation of the fragment.

result shown in the diagram of figure 6*A*. Restorations of the probable thickness and curvature of the articular cartilage prior to the separation is shown in figure 6*B*, the inferior dotted line representing the deep surface of the articular cartilage. In this diagram, the buckled fragment is placed in position with the deep surface of the cartilage coinciding with the reconstructed line of the original deep surface. In figure 6*C*, the fragment is represented as roughly restored to its original contour, revealing a considerable unfilled space and forcing the conclusion that a "cyst" existed in this situation before the separation of

and the stellate ganglion together with the resection of that portion of the vagosympathetic trunk which has included in it the middle cervical ganglion

2 Section of the extrinsic nerves that lead to one lung does not cause any change in the frequency or character of the respiratory movements

3 The partially denervated lung reacts as its normal mate to all forms of stimulation

4 The carbon dioxide combining power of the blood plasma remains unchanged after partial denervation of one lung

5 Section of the extrinsic nerves that lead to one lung does not prevent the occurrence of a typical massive atelectasis (collapse) of that lung

6 The ganglions situated in the bronchial walls remain intact after the most extensive operation that is directed to produce complete denervation of one lung, consequently, it is technically impossible to obtain a complete denervation of either lung

7 Because of the persistence of the peripheral ganglions, there will probably always be a few failures from the surgical treatment for bronchial asthma, regardless of which operative procedure has been carried out

the fragment. The reason for the buckling of the bone and cartilage comprising the fragment is thus accounted for. The change in the curvature of the articular surface of the condyle may also be explained on the basis of the yielding of the bone deprived of support by the absence of a considerable volume of cancellous structure as represented by the several cysts.

The buckling of the fragment probably was the first important mechanical consequence of the change in shape of the cartilage yielding under pressure, and suggests the consequences of lateral stress, a warrantable inference is that the cyst into which the fragment collapsed was originally considerably greater in its lateral (horizontal, anteroposterior) dimensions.

Another inference drawn because of the absence of recognizable new bone formation in the crater is that along the line of separation of the fragment this cyst extended close to the deep surface of the articular cartilage.

On the basis of the microscopic and gross study of the sections, we venture to offer the following explanation of the specimen of osteochondritis dissecans which came into our hands.

The separation was the effect of mechanical pressure on a portion of the articular cartilage with underlying cancellous bone bridging a "cyst." This pressure probably was intermittent, as occasioned by variation in functional performances of the joint, and probably was the resultant of stresses operating roughly in the long axis of the bone and laterally in the anterior-posterior direction. The lateral stresses are suggested by the change in convexity of the articular surface and the presence of large defects in cancellous bone deep to the lesion. The effects of the loss of the cancellous bone in volume represented by the cysts we think are shown by the shortening of the anteroposterior diameter of the condyle, as shown in figures G, I, H, and C, and by the buckling of the fragment.

There are two essentials to our explanation—one, a sufficient loss in the condyle of cancellous bone to weaken materially the support of the articular cartilage as a whole. The other, the presence of a "cyst" immediately below the articular cartilage in a position subject to vertical and horizontal stresses.

The rarity of typical instances of osteochondritis dissecans of the femur suggests that our explanation, even in dependence on the numerous cysts and distribution of cysts" may apply to other examples.

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# OSTEOCHONDRITIS DISSECANS \*

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AND  
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The present study was made on a specimen removed at autopsy. The patient was reported to have died of diabetes mellitus. During the progress of the autopsy, the knee was discovered to be slightly swollen. Clinical symptoms of trouble with the knee were not recorded, but when the knee was opened, a typical instance of osteochondritis dissecans was found.

The discovery of loose bodies within a joint, especially the knee, has been of great clinical interest, both in respect to the origin of these bodies and as regards treatment. Various names have been used to describe them, such as "joint mouse," "loose body," "floating body" and others. There are several varieties, namely, those which result from a disease process, such as tuberculosis, tabes or pus infection, those which follow definite trauma, wherein a portion of bone and cartilage is broken off, those which result from proliferative changes in the cartilage or synovial membrane as a result of arthritis, and lastly, those in which the origin is obscure or only partially explainable.

It is the latter class which concerns us in this study.

## CLINICAL COURSE

In certain instances with or without recognized trauma, patients develop a symptom complex which suggests that there is a loose body in one of the joints. By far the most frequently affected joint is the knee. The symptoms complained of are usually slight swelling, slight discomfort and at times, locking of the joint. Roentgenographic study will at times reveal the loose body, either free in the joint or attached to the articular surface (figs 1 and 2). Operative removal is indicated. At operation, the loose body is picked out of the articulation. It may be freely movable in the joint cavity, or it may still be resting in its bed. Examination of the body will show a surface of articular cartilage, oval or rounded, with clearcut edge, and an under surface of the subcartilaginous cancellous bone. This body will exactly fit into a defect in the surface of the articular cartilage, the craterlike defect

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will also have a clearcut edge of cartilage, with a base more or less filled with fibrous tissue, depending on the period of time which has elapsed since the body fell out of its bed

This type of loose body in a joint is that which Koenig has described as "osteochondritis dissecans" It occurs most frequently in the internal condyle of the femur, but it also has occurred in the elbow, the hip

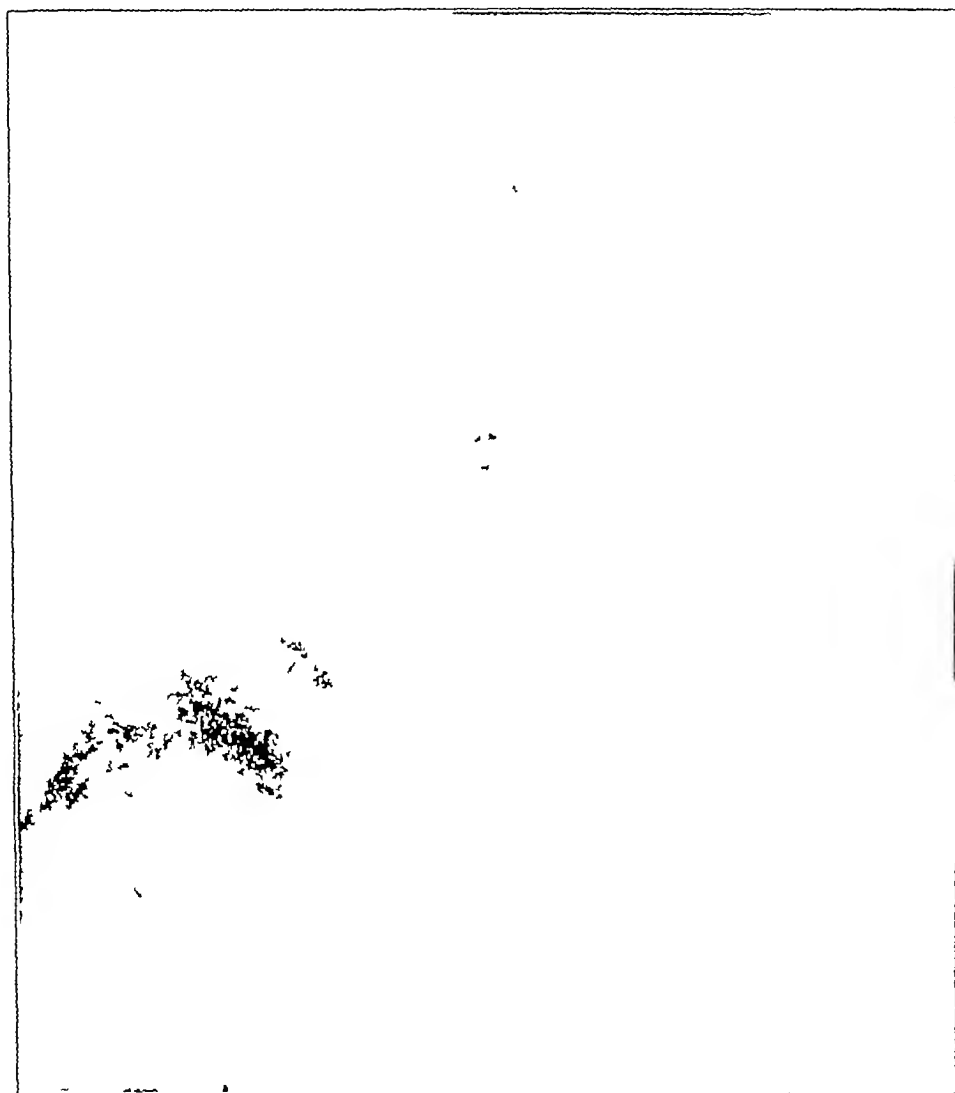


Fig 1—Osteochondritis dissecans, The loose body is clearly shown in the lateral plane

and the shoulder joints It is to be remembered that these joints do not present any other evidence of disease process, nor are there constitutional disturbances present, such as elevation of temperature or illness, locally, signs of inflammatory process, such as heat and redness, are not seen, the pain and swelling present being due to joint irritation of a mechanical nature





## OBSERVATIONS ON THE CAUSATION OF LOOSE BODIES IN JOINTS

About 250 years ago Pechlin studied and, in a way, described the various types of loose bodies in joints. In 1726, Monroe advanced the theory that trauma plays an important rôle in the formation of loose bodies. In 1848, Raney observed that fragments of cartilage



Fig 2—Same as figure 1, taken in the anteroposterior plane. The loose body at the surface of the internal condyle is less clearly indicated.

and bone detached within the joint by trauma continued to grow and become sizable loose bodies, regardless of their parent structure. In 1851, Rokitsansky stated his belief that bodies composed of bone and cartilage might arise from the articular serosa, representing an excessive development and ossification of isolated nodules of cartilage. John Hunter believed that loose bodies within a joint were at first blood

and mucoid tissue in the thyroid tumors does not appear to be a degenerative process, but a part of the life history of the tumor. The term "mixed tumor" is properly applied to those ovoid growths which are found within the normal or goitrous thyroid gland, the structure of which resembles that of the underdeveloped gland. Its chief gross characteristics are the uniform ovoid shape, the division into reniculi-like pyramids, often with central areas of fibrous tissue, and its definite encapsulation.

Closer acquaintance with this tumor is desirable, because it has a life history of its own, and because it has been constantly and persistently confused with the nodules commonly found in lobulated colloid goiters. This confusion has been so complete that many writers believe that the nodulations of the old colloid goiters go through a stage simulating or identical with that of the so-called fetal adenomas. The delusion is at once apparent when the structure of small mixed tumors are compared with the interacinar new formation of glands.

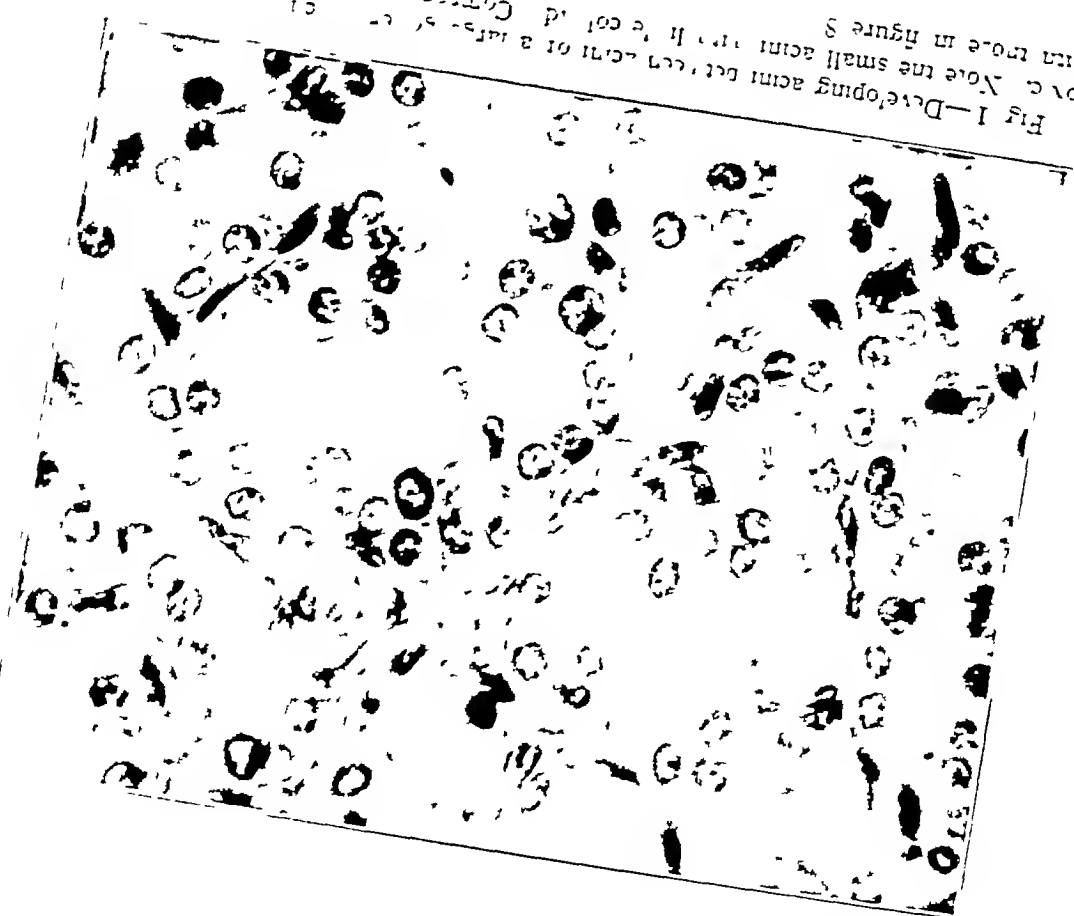
The actual source of these tumors is not known. Clinically they are commonly seen in young persons, when they are no larger than a hazelnut. Wölfler assumed that they are derived from certain groups of cells of fetal origin situated in the interstices between the acini of goiters of glands typical of these tumors, but whether or not the beginnings of the tumors are in such islands is not known. Most authors who have published illustrations of these alleged islands have presented only high magnifications of a few glands, making it impossible to judge of the topography of the environment. Any one with a willing disposition and a high power lens can prove almost anything particularly if it is "von Verfasser gezeichnet." As a matter of fact, such groups of cells (fig 1) are frequently found in glands that show a beginning toxicity. But they are multitudinous (fig 2), and one would have to assume that each of these areas may be the point at which the future adenoma will develop. True enough, areas identical with the fetal adenoma are found in goiters now and then (fig 3). I have encountered such islands in less than one half of 1 per cent of goiters. Furthermore, most of these little islands showed evidence of degeneration, indicating that they have failed in development and are not potential tumors of magnitude. Those who assume that each hypothecate something unusual in ontogenesis. The multiple origin of true tumors should not be hypothesized without the backing of definite evidence, a thing wholly lacking in this connection.

clots which became organized and attached to articular cartilage, and which assumed its characteristics. Laennec's (1854) theory was that following an arthritis, cartilage might develop in the thickness of the fibrous capsule or in the synovial tissue, and that it might develop the structure of articular cartilage. Paget believed that loose bodies were sequestrums which followed a "quiet necrosis" localized in the base of the articular cartilage. He believed that trauma did not play any part in causation. Journeaux and Hermann (1889) produced evidence of the synovial origin of certain types of loose body, and they believed that synovial cells might take on the characteristics of cartilage cells. Poulet and Villard, at about the same time, expressed the belief that loose bodies in joints were always due to a condition known as "dry arthritis." In 1887, Koenig wrote his description of a distinct pathologic entity which he called "osteochondritis dissecans." He believed that this was an inflammatory lesion of unknown origin, which resulted in the occlusion of the terminal arteries supplying an area of the articular cartilage on the mesial condyle of the femur, producing a separation of a small area of cartilage, and that this area dropped out of the surface of the cartilage with a shell of subchondral bone attached, thus becoming a loose body in the joint space. Koenig realized that trauma might act as a causative factor. His description and explanation aroused considerable controversy. Lever (1910) advanced the view that certain loose bodies might arise from "embryonic rests" of cartilage cells. Freiburg (1910) reported several well studied cases, and stated his belief that Wollenberg's vascular theory offered a full explanation of the origin of loose bodies. Anhausen (1924) confirmed Koenig's observations as to origin, and drew a forcible comparison between the loose bodies in the knee, in the elbow and in the hip and the osteochondritis known as Legg-Perthe's disease, Kohler's disease of the metatarsal head and tarsal scaphoid. He believes that a slow absorption and necrosis start in the epiphysis and develop into a line of demarcation composed of granulation tissue which is replaced by fibrous tissue. An intercurrent injury jars the loose piece of cartilage loose from its bed. The primary cause is either trauma to smaller blood vessels of the epiphysis or a benign type of emboli lodging in the terminal vessels of the epiphysis.

Timbrell Fisher (1924) showed by experiments on animals that trauma to the epiphysis will produce a low grade type of inflammatory process in a certain area, which thus has lowered vitality and which may be gradually extoliated. Many observers, notably Codman, have experimented in the production of the actual lesion of osteochondritis dissecans by striking the femoral condyle with a hammer. The lesion may be produced thus in the knee of a cadaver.



Fig 1—Developing acini cell, center of a large, solid, cortical, and cortical, with more in figure 3  
 Note the small acini with the solid, cortical, and cortical, with more in figure 3



plasia—had occurred during an exacerbation in sympathy with the remainder of the parenchyma, it would seem likely that the nodules were of similar origin. In this study, 34 per cent of the cases tell in this group. In a previous study, fifty such cases were reported. The histologic changes of hypertrophy and hyperplasia which occurred throughout the gland also involved the hypervoluted parenchyma forming the nodules and clinical tumors. This involvement did not occur in 8 per cent of the cases of true neoplasms.

In 1905, MacCallum<sup>2</sup> first called attention to the fact that in cases of exophthalmic goiter the histologic changes denoting hypertrophy and hyperplasia might be confined to "small patches here and there throughout a gland which otherwise seems normal. Microscopically, the altered areas are quite sharply demarcated from the rest and may involve a great number of alveoli or be limited to very small foci, including only a few alveoli here and there." The cases originally studied by MacCallum were included in the Johns Hopkins Hospital, and his original observations were confined, not only for the cases up to 1905, but also for those from 1905 to 1927. Hence it would appear certain that in hypertrophism, hypertrophy and hyperplasia of the parenchyma may occur only in certain regions and in certain lobules of acini, or it may involve the thyroid gland diffusely and as a whole. The only difference in the clinical manifestations of the cases associated with diffuse involvement of the gland and those in which only certain well defined areas were affected by the morbid process was that the latter group as a rule was of a milder type. It has been pointed out that the most severe cases of hypertrophism, in which the entire thyroid gland is involved in the pathologic hypertrophy and hyperplasia of the parenchyma undergo artificial and spontaneous remissions associated with a histologic transformation that is characterized by involution, regression and actual disintegration of the parenchyma. Therefore, when the pathologic hypertrophy and hyperplasia are limited to certain specific areas of the gland it would be expected that the involutional changes associated with clinical remissions, whether artificial or spontaneous, would also be limited to these areas. This was true in 58 per cent of the 107 cases of the present study, in which there was a nodular goiter associated with a low grade clinical hypertrophism of long standing. In these cases the thyroid glands were examined at the height of an exacerbation. It was found that the nodular elements were composed of the same parenchyma in which the histologic changes associated with the morbid phase of the disease cycle, i.e. hypertrophy and hyperplasia, were

<sup>2</sup> MacCallum W. G. MacCallum's Text-Book of Pathology, 1905, published by W. B. Saunders Company, p. 1014.

simultaneously with those alterations in the microscopic structure concomitant with involution of a previous hypertrophy and hyperplasia. The parenchyma intervening between these nodules had the appearance of normal thyroid tissue. Thus, it would seem that the disease, hyperthyroidism, pathologically may be divided into two phases: an active phase associated with the histologic changes denoting hypertrophy and hyperplasia, and an artificial or spontaneous, less active phase associated with involution of the hyperplastic parenchyma. The disease cycle and its associated morbid pathologic process may involve the entire thyroid or only portions or specific and well defined areas of the gland.

Formerly, only the pathologic changes in the thyroid (hypertrophy and hyperplasia) associated with the active stage of the disease were recognized mainly because the patients were either operated on at the height of an exacerbation or died during a fulminating stage of the disease. A check between the clinical severity and the histologic structure became possible with the advent of the determination of the basal metabolic rate and the reintroduction of the use of iodine in the treatment of patients with hyperthyroidism. Under these circumstances, it has become necessary to change one's ideas in regard to the histologic alterations encountered in the thyroid in cases of hyperthyroidism. Whereas, before, the presence of large cysts, encapsulated areas of dilated colloid-containing acini and diffuse scarring were little understood, their pathogenesis can in the light of the now known involutional changes, be rationally explained. For years all nodules or lumps in the thyroid have been termed "adenomas," because encapsulated sharply defined areas of hyperplastic thyroid parenchyma, associated with histologic regression or disintegration and fibrous tissue substitution differed in its pattern from the old ideas of the histologic structure of exophthalmic goiter.

When analyzed in the present state of our knowledge, the nodules in this group of sixty-three cases were found to be composed of thyroid parenchyma in an active state of hypertrophy and hyperplasia associated with the microscopic changes characteristic of involution. Depending entirely on the duration of the disease or on the number of times the disease cycle has been completed, the involutional changes, such as fibrosis, or central acinar disintegration with deposition of colloid and cyst formation, will be in evidence. Thus, in older people in whom the disease process has extended over a long period of time, the extent of histologic regression will be greater in these areas, the encapsulation more pronounced and the nodules larger. In some of these nodules only a small rim of thyroid tissue remains. In our series of controlled cases, the process of hypertrophy and hyperplasia was apparently attended with an enlargement of the whole thyroid, which was again increased during involution owing to the deposition of colloid. It

The development of the common uniform colloid goiter into the nodular type can be easily traced from the formation of new acini in the interstitial cells and from the walls of the old acini, as discussed in my previous paper

Ribbert declared that fetal adenomas are seldom seen in children. I find them commonly in small children, usually in the absence of enlargement of the gland proper. In the soft goiters of adolescents, they are often conspicuous as small firm nodules easily detected in the softer tissue of the goitrous gland. That they are something apart



Fig 3—Small "fetal adenoma" in an old colloid goiter only recently becoming toxic. The nodule, tiny as it is, shows degeneration indicating its age.

from the goiter proper is shown by the fact that they are not influenced by treatment. They never become smaller as the goiter as a whole approaches the normal.

These tumors are nearly always solitary and commonly exist as the only thyroid lesion. Their encapsulation causes them to be definitely separated from the surrounding tissues, causing them to be freely movable. Their capsules, however, are nearly always definitely suffused with the capsule of the thyroid gland. The gland about them is pushed to one side by the growth of the tumor. Because these tumors have been confused with the bossilations of old colloid goiters, this characteristic has been ascribed to all so-called "adenomas." It is only these



## CONCLUSIONS

- 1 Mixed tumors are true tumors of the thyroid gland
- 2 They are comprised of acini more or less characteristic of immature thyroid tissue
- 3 The fibrous tissue is prone to have a characteristic keloid-like proliferation and mucoid degeneration
- 4 The acini may develop colloid and later undergo the changes of an old colloid goiter, leading to toxicity. The toxicity never reaches the degree of a true exophthalmic goiter
- 5 The tumors may menace the life of the patient by a hemorrhage into their substance
- 6 They may undergo active acinar proliferation leading to malignancy



Fig. 4—Cross-section of a typical mixed tumor. The ovoid form, the central fibrous core and the indefinite division into lobules are well shown.



Fig. 5—The entire tumor and a cross-section of the same. The central core is cystic and there is an irregular cystic area to the left of the center.



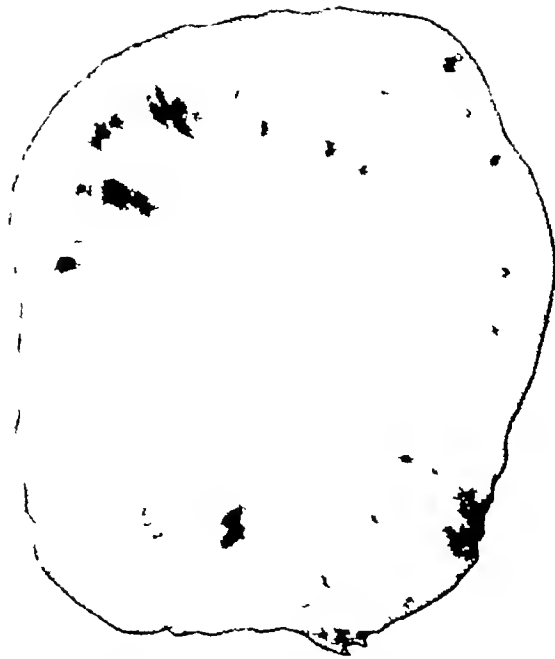


Fig 6—Tumor with extensive central fibrous area with the renacula-like areas about the periphery



Fig 7—Large bossiated colloid goiter showing the innumerable small nodules. In order to fit this into the "adenoma" theory it is necessary to hypothecate a separate focus of origin for each nodule

good and she was allowed to walk about. On August 2, while walking, she began to feel weak. The dressings became saturated with blood, and she died almost immediately.

*Autopsy Report*—The autopsy was performed the following day by Dr Paul Klemperer. The most important facts are given from the complete report. There was a healing thoracotomy wound in the right side of the back with resection of



Fig 1—The polypoid growth attached to the lateral wall and partly filling the lumen of the bronchus of the lower lobe. The probe is introduced into the tear of the aneurysmatic pulmonary artery branch within the wall of one of the bronchiectatic cavities distal to the neoplasm.

several ribs. In the base of the wound there appeared several lumina from which blood exuded on pressure. The right lung was firmly adherent to the wall of the chest and was removed with difficulty. The right lung weighed 550 Gm, the left, 310 Gm. On opening the lung (from behind), the bronchi of the upper and middle

mixed tumors that push the gland aside. The bossilations of the old colloid goiters are part of the once diffusely enlarged gland, and there is no normal gland to be pushed aside, or to be saved at operation, as every discerning surgeon knows.

More important than any theory as to origin is the structure of the tumor itself.

### PATHOLOGIC ANATOMY

The most striking characteristic of the tumors is their constant ovoid shape, whether they exist alone or as a part of a nodular colloid goiter (fig. 4), less often they are spherical (fig. 5). They are never lobulated and they are nearly always solitary. They are firm to the feel and are generally elastic. When they have undergone degeneration, they may be soft or fluctuant.

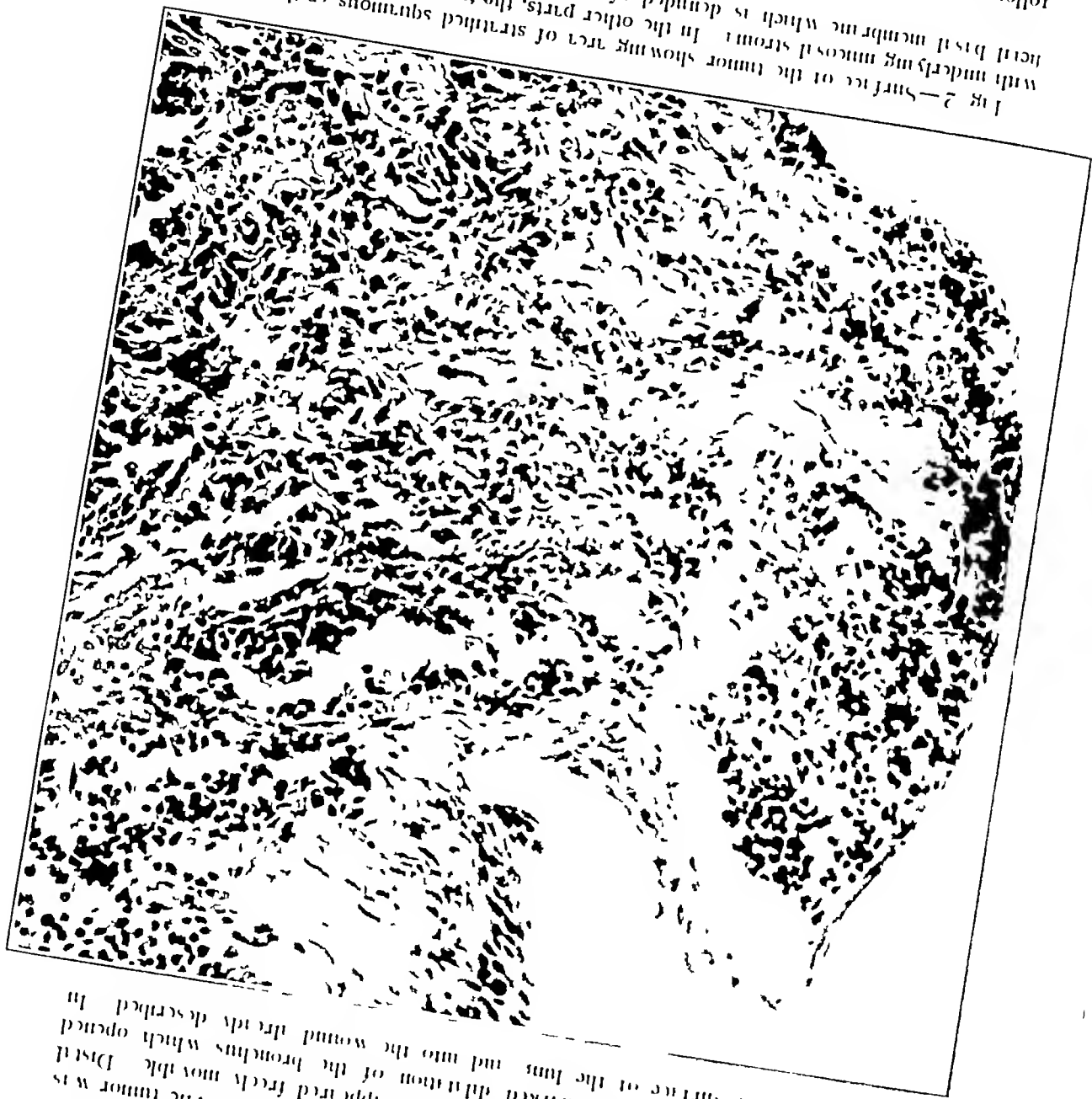
On section, they are found to be deep red, unless they have undergone secondary degeneration. They are commonly divided into separate pyramidal lobules, the apexes of which point to a common center like the divisions of a grapefruit (fig. 4). In most of them, there is a white core, usually stellate. This core may form only a small nucleus in the center, or it may occupy the larger part of the tumor (fig. 6). This arrangement of the small lobulations with the white center is sufficient to differentiate them from the nodules of a colloid goiter (fig. 7). In many of the older ones various forms of degeneration are noted, this degeneration is usually cystic, but is often colloid and sometimes hemorrhagic. These tumors are always surrounded by a heavy connective tissue capsule, heavier than the true capsule of the normal thyroid gland.

### HISTOLOGY

Figure 8 shows the tumor to be made up of closely packed acini. In the younger specimens, few or none contain colloid. The cells are small and closely packed; the nucleus is spheroidal and the protoplasm deeply staining. It is interesting to compare the structure of the salivary mixed tumors with such pictures (fig. 9). In the older ones, the colloid is small in amount, acidophilic and without vacuolization, even in specimens fixed in a solution of formaldehyde. As the tumors grow older the acini may all contain colloid and the slide may resemble closely the acini of the old colloid goiter (fig. 10).

The most striking and constant picture of these tumors is to be seen in the central stellate area already mentioned. The centers are always made up of heavy bundles of fibrous tissue, recurrently bedecked with a few inflammatory cells. They are round, except in the older and degenerated specimens, take the dye poorly or not at all. These areas are usually partially or wholly unenclosed by the connective tissue between the acini (fig. 11).

Fig. 2.—Surface of the tumor showing area of stretched squamous epithelium with underlying mucosal stroma. In the other parts, the tumor reaches the superficial membrane which is divided of epithelium,  $\times 80$ .



lobes of the right lung were found to be normal. Within the lumen of the main bronchus of the lower lobe of the right lung there appeared a cylindrical pedunculated tumor which measured 21 mm by 6 mm (Fig. 1). The tumor was attached to the lateral wall of the bronchus and appeared freely movable. Distal from the tumor there was marked dilation of the bronchus which opened directly on the surface of the lung and into the wound already described. In



Fig 8—Slide from a mixed tumor of ten years' duration *A* indicates an area near the periphery showing the small acini some of which are beginning to accumulate colloid, *B*, an area nearer the center of the tumor showing the developing mucoid tissue between the acini

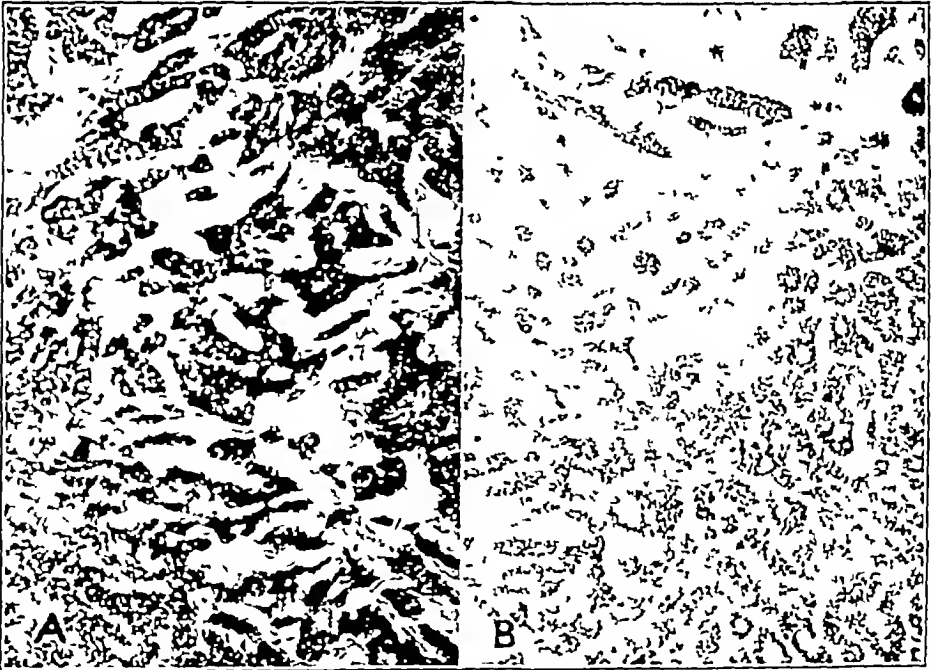


Fig 9—Comparison with figure 8, a mixed tumor of the submaxillary gland of eight years' duration *A* indicates an area near the periphery, *B*, an area near the center showing wide areas of mucoid material



vessel was an aneurysmal dilatation. In the upper lobe of the right lung and in the left lung no changes were found except aspiration of blood.

*Pathologic Anatomic Diagnosis*—The diagnosis was as follows: polypoid tumor of the main bronchus of the lower lobe of the right lung with partial occlusion of the lumen, multiple sacculated bronchiectases in the distal ramifications of the bronchus with bronchopleural fistulae, and rupture of an aneurysmal dilatation of a pulmonary artery branch with subsequent severe hemorrhage.

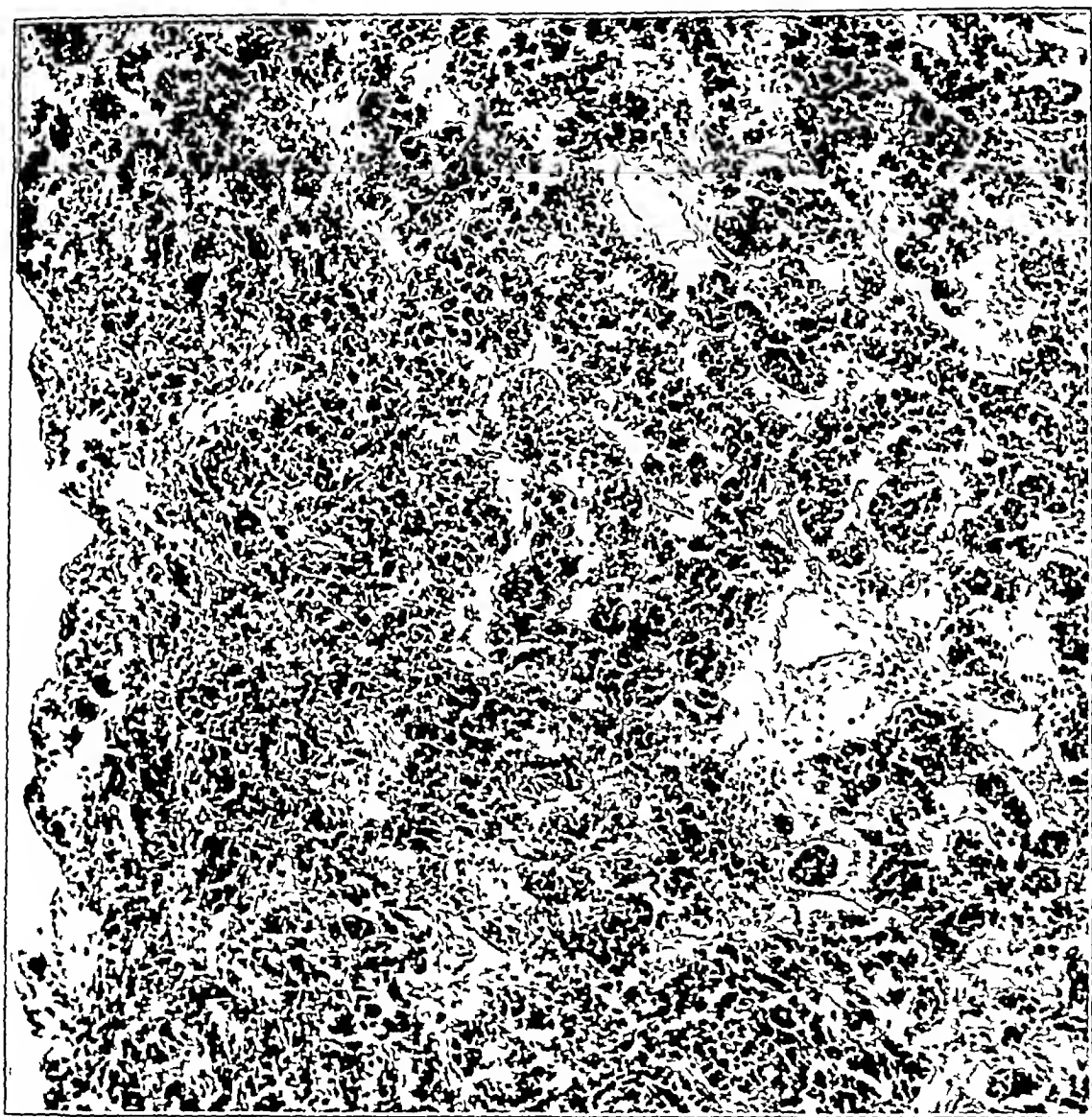


Fig 3—General view of the tumor showing its distinct glandular architecture,  $\times 40$

*Microscopic Examination of the Tumor*—Sections were taken from the surface as well as from the pedicle of the tumor. On the surface there was occasionally a stratified layer of squamous epithelium (fig 2), occasionally there was seen a single layer of columnar epithelium. Mostly, however, the surface was denuded of epithelium due to postmortem desquamation. The epithelium rested

Wolfler assumes that they result from the organization of blood clots. There is no evidence for this assumption. In the first place hemorrhages due to a pathologic process do not organize in a regular manner, because they do not form a true clot. Then, too, when blood clots do organize, they do not form bundles such as are seen here continuous with the normal struma of the gland. Furthermore the fibers of these masses are like the stroma of the tumors in tinctorial reaction. It appears fair to assume that for some reason the tissue forming the core of these tumors is prone to this keloidlike proliferation and forms an essential part of the life history of the tumor.

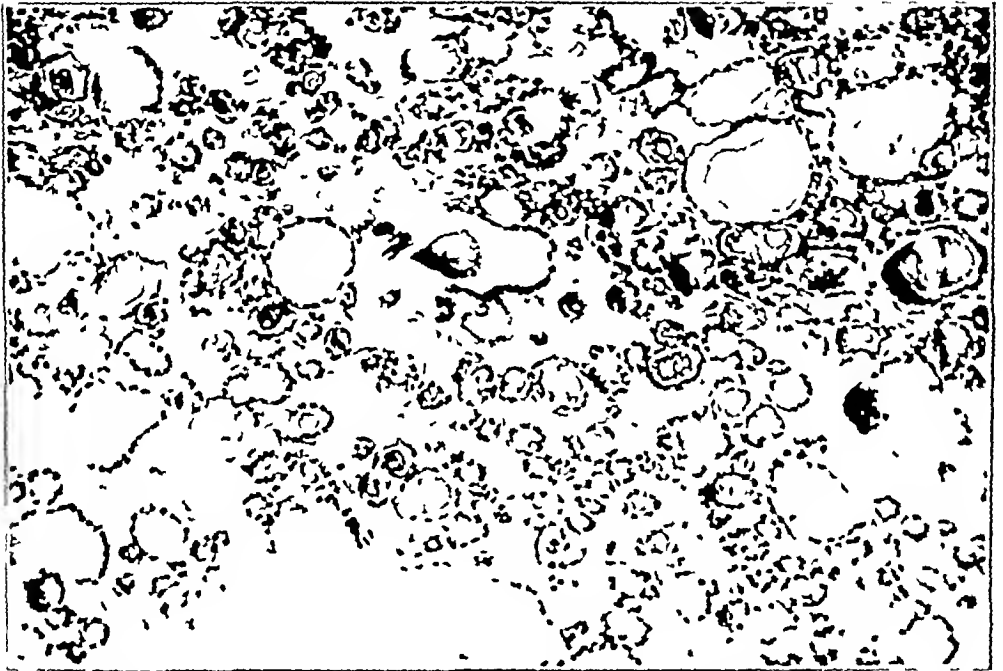


Fig. 10—Old mixed tumor showing large acini containing colloid. This patient had mild toxic symptoms.

The connective tissue between the acini undergoes a degeneration peculiar to these tumors. It becomes abundant and stains poorly, or not at all. The acini are sparse, isolated and often atrophic (fig. 12).

These tumors become larger in the course of time either by the formation of new acini with accumulated colloid or by the formation of connective tissue or both. In their terminal stages they may develop degenerative changes and become cystic through softening of the tissue with or without added hemorrhage. These tumors tend either to belated initiation of a colloid goiter by developing follicles and manifestation of hyperactivity or they tend to the formation of malignant tumors.

The gland may take on a belated development and recede to a colloid goiter. The acini become large and filled with colloid, and

the sections. The tumor appeared to be composed of round and oval alveoli epithelial cells which rest everywhere on a basement membrane, X 200  
 often intercommunicating and lined by columnar epithelium which contained a cylindrical rather dark nucleus. The cells rested on a basement material, apparently inus (fig 5). The stroma was composed of loose connective tissue and showed occasional infiltration with polymorphonuclear leukocytes, plasma cells and lymphocytes and contained numerous thin-walled blood vessels.

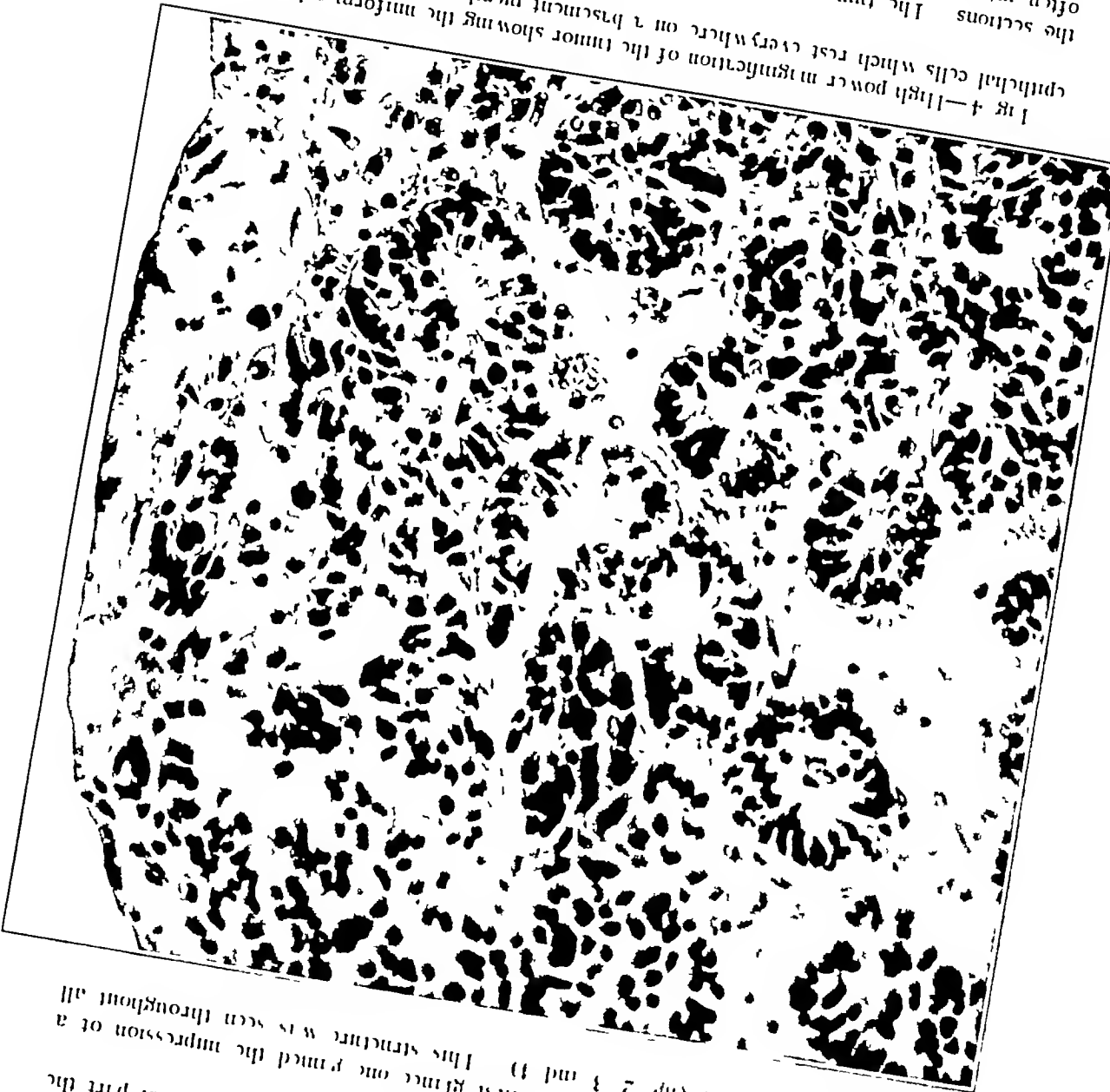


Fig 4—High power magnification of the tumor showing the uniform columnar epithelial cells which rest everywhere on a basement membrane, X 200  
 on a basal membrane which could be followed up along the entire circumference of the tumor except at the points where the cut section was carried. Beneath the basal membrane there was a rather wide liver composed mainly of elastic fibers. This liver however, could be seen only in a few places, for the most part the tumor extended up to the surface.  
 As to the tumor proper, if the first plane one found the impression of a glandular structure (fig 2, 3 and 4). This structure was seen throughout all



Fig 11—Area of the fibrous tissue core showing the heavy fibrin bundles. These fibers are seen to be continuous with the fibers extending between acini with mucoid areas between the fiber bundles (Mallory's phosphotungstic acid stain)



Fig 12—Slide showing some large acini filled with colloid together with many smaller ones. Between the acini are fine fibrils the interstices or which is occupied by mucoid material (Mallory's phosphotungstic acid stain)

On close examination, variations in the structure of the alveoli as well as variations in the cells could be seen distinctly. It was striking that the alveolar structure was more clearly demonstrated in the peripheral portion of the tumor than in the central one. While the cells in the peripheral portion were uniform in appearance, those in the central part differed considerably (fig 6), they were larger and contained large dark nuclei, the nucleocytoplasm ratio being altered to the disadvantage of the latter. Cells with two and more nuclei and occasional

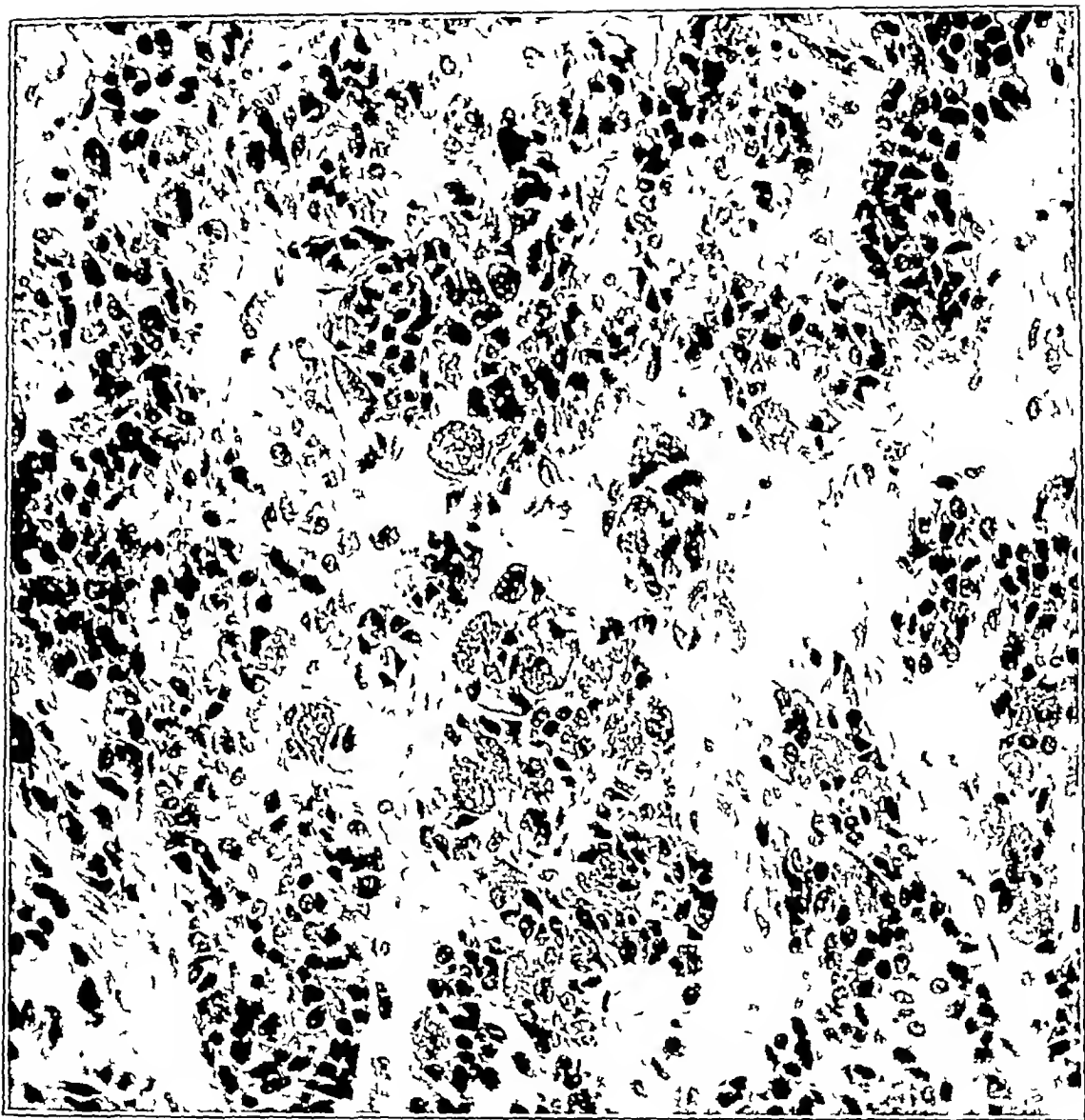


Fig 5—A portion of the tumor with mucus secretion within the alveoli,  $\times 160$

mitoses were found. Sections from the pedicle of the tumor did not show any infiltration of the bronchial wall. From this description it can be concluded that the tumor originated from beneath the bronchial mucous membrane, since it was surrounded in its entire circumference by the basement membrane and the surface epithelium was still

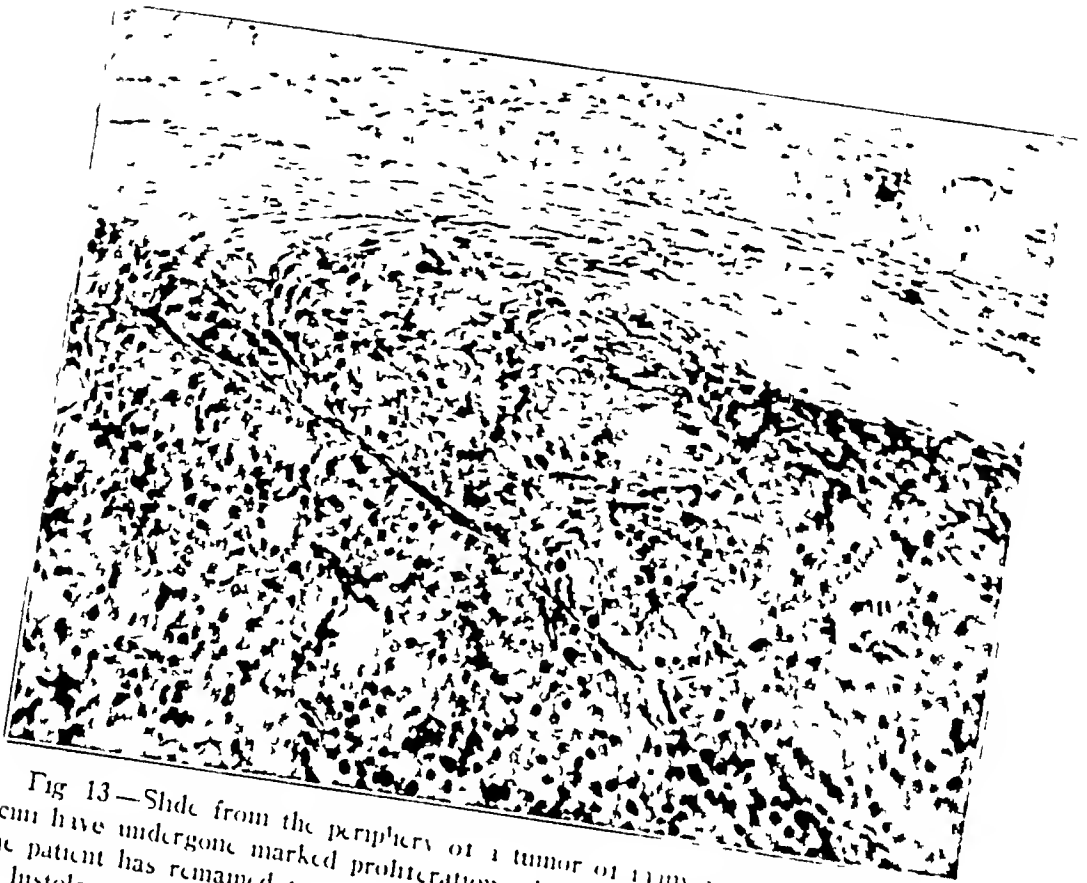


Fig 13—Slide from the periphery of a tumor of many years duration. The tumor has undergone marked proliferation; the capsule was not perforated and the patient has remained free from recurrence, but the tumor must be regarded as histologically malignant.



1. 14-16-17-18-19-20-21-22-23-24-25-26-27-28-29-30-31-32-33-34-35-36-37-38-39-40-41-42-43-44-45-46-47-48-49-50-51-52-53-54-55-56-57-58-59-60-61-62-63-64-65-66-67-68-69-70-71-72-73-74-75-76-77-78-79-80-81-82-83-84-85-86-87-88-89-90-91-92-93-94-95-96-97-98-99-100-101-102-103-104-105-106-107-108-109-110-111-112-113-114-115-116-117-118-119-120-121-122-123-124-125-126-127-128-129-130-131-132-133-134-135-136-137-138-139-140-141-142-143-144-145-146-147-148-149-150-151-152-153-154-155-156-157-158-159-160-161-162-163-164-165-166-167-168-169-170-171-172-173-174-175-176-177-178-179-180-181-182-183-184-185-186-187-188-189-190-191-192-193-194-195-196-197-198-199-200-201-202-203-204-205-206-207-208-209-210-211-212-213-214-215-216-217-218-219-220-221-222-223-224-225-226-227-228-229-230-231-232-233-234-235-236-237-238-239-240-241-242-243-244-245-246-247-248-249-250-251-252-253-254-255-256-257-258-259-260-261-262-263-264-265-266-267-268-269-270-271-272-273-274-275-276-277-278-279-280-281-282-283-284-285-286-287-288-289-290-291-292-293-294-295-296-297-298-299-300-301-302-303-304-305-306-307-308-309-310-311-312-313-314-315-316-317-318-319-320-321-322-323-324-325-326-327-328-329-330-331-332-333-334-335-336-337-338-339-340-341-342-343-344-345-346-347-348-349-350-351-352-353-354-355-356-357-358-359-360-361-362-363-364-365-366-367-368-369-370-371-372-373-374-375-376-377-378-379-380-381-382-383-384-385-386-387-388-389-390-391-392-393-394-395-396-397-398-399-400-401-402-403-404-405-406-407-408-409-410-411-412-413-414-415-416-417-418-419-420-421-422-423-424-425-426-427-428-429-430-431-432-433-434-435-436-437-438-439-440-441-442-443-444-445-446-447-448-449-450-451-452-453-454-455-456-457-458-459-460-461-462-463-464-465-466-467-468-469-470-471-472-473-474-475-476-477-478-479-480-481-482-483-484-485-486-487-488-489-490-491-492-493-494-495-496-497-498-499-500-501-502-503-504-505-506-507-508-509-510-511-512-513-514-515-516-517-518-519-520-521-522-523-524-525-526-527-528-529-530-531-532-533-534-535-536-537-538-539-540-541-542-543-544-545-546-547-548-549-550-551-552-553-554-555-556-557-558-559-560-561-562-563-564-565-566-567-568-569-570-571-572-573-574-575-576-577-578-579-580-581-582-583-584-585-586-587-588-589-590-591-592-593-594-595-596-597-598-599-600-601-602-603-604-605-606-607-608-609-610-611-612-613-614-615-616-617-618-619-620-621-622-623-624-625-626-627-628-629-630-631-632-633-634-635-636-637-638-639-640-641-642-643-644-645-646-647-648-649-650-651-652-653-654-655-656-657-658-659-660-661-662-663-664-665-666-667-668-669-670-671-672-673-674-675-676-677-678-679-680-681-682-683-684-685-686-687-688-689-690-691-692-693-694-695-696-697-698-699-700-701-702-703-704-705-706-707-708-709-710-711-712-713-714-715-716-717-718-719-720-721-722-723-724-725-726-727-728-729-730-731-732-733-734-735-736-737-738-739-740-741-742-743-744-745-746-747-748-749-750-751-752-753-754-755-756-757-758-759-760-761-762-763-764-765-766-767-768-769-770-771-772-773-774-775-776-777-778-779-780-781-782-783-784-785-786-787-788-789-790-791-792-793-794-795-796-797-798-799-800-801-802-803-804-805-806-807-808-809-810-811-812-813-814-815-816-817-818-819-820-821-822-823-824-825-826-827-828-829-830-831-832-833-834-835-836-837-838-839-840-841-842-843-844-845-846-847-848-849-850-851-852-853-854-855-856-857-858-859-860-861-862-863-864-865-866-867-868-869-870-871-872-873-874-875-876-877-878-879-880-881-882-883-884-885-886-887-888-889-890-891-892-893-894-895-896-897-898-899-900-901-902-903-904-905-906-907-908-909-910-911-912-913-914-915-916-917-918-919-920-921-922-923-924-925-926-927-928-929-930-931-932-933-934-935-936-937-938-939-940-941-942-943-944-945-946-947-948-949-950-951-952-953-954-955-956-957-958-959-960-961-962-963-964-965-966-967-968-969-970-971-972-973-974-975-976-977-978-979-980-981-982-983-984-985-986-987-988-989-990-991-992-993-994-995-996-997-998-999-1000-1001-1002-1003-1004-1005-1006-1007-1008-1009-1010-1011-1012-1013-1014-1015-1016-1017-1018-1019-1020-1021-1022-1023-1024-1025-1026-1027-1028-1029-1030-1031-1032-1033-1034-1035-1036-1037-1038-1039-1040-1041-1042-1043-1044-1045-1046-1

base. Microscopically, the presence of the basement membrane supports the gross diagnosis of the benign nature. The deeper portions of the bronchial mucous membrane were compressed, but the basement membrane and the overlying epithelium was still preserved and nowhere had it been perforated. This pointed to an expansive and not an infiltrative growth, which was also in accord with

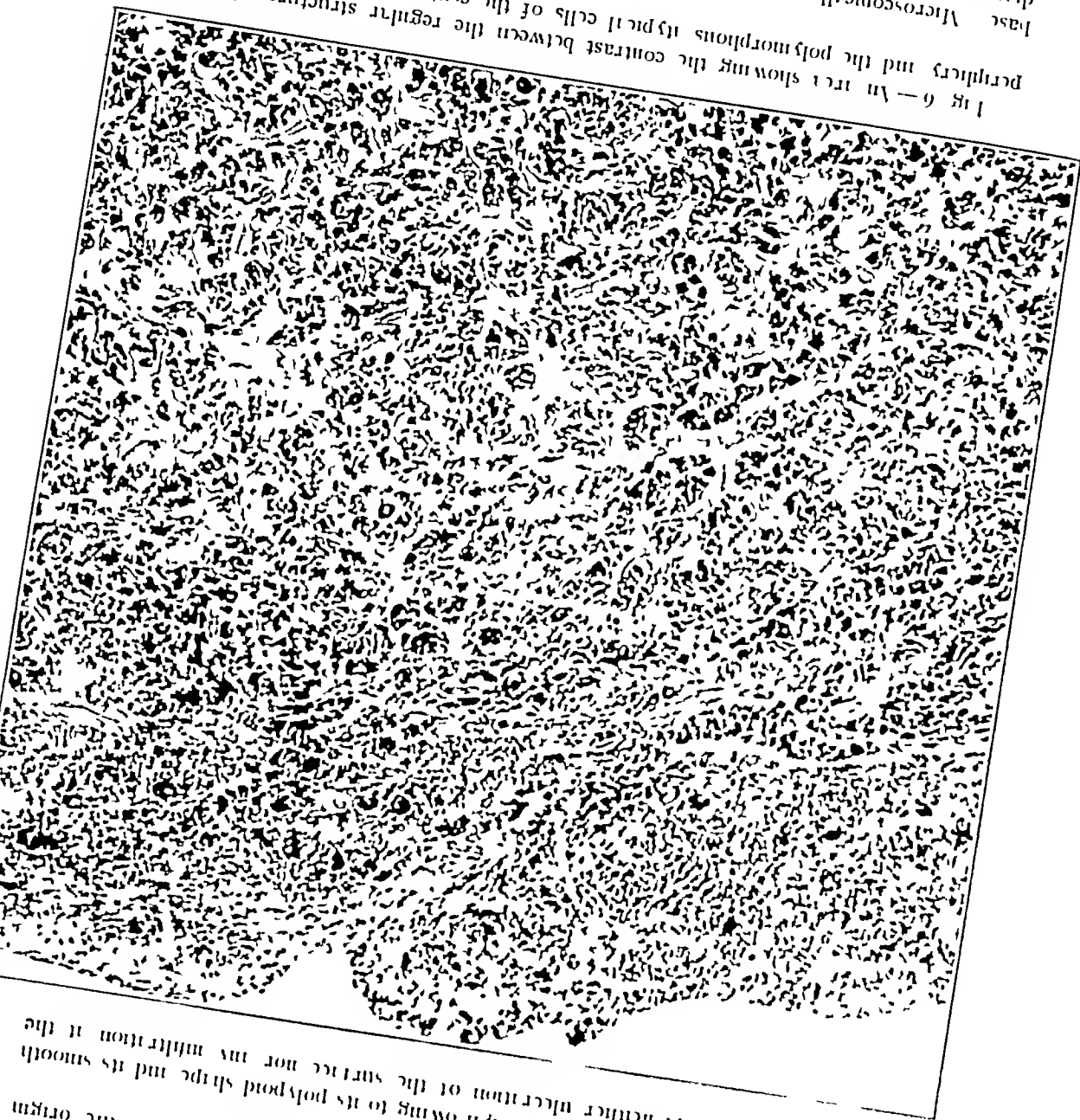


Fig 6—An area showing the contrast between the regular structure of the periphery and the polymorphous typical cells of the central portions, X 40

preserved in places. Therefore, it might have originated either from the mucous glands or from their excretory ducts. The columnar shape of the cells composing the alveoli and the fact that only occasional accumulations of mucus are encountered and the intercommunication of the alveoli, speak in favor of the origin from the excretory ducts.

Grossly, the tumor appeared benign owing to its polypoid shape and its smooth surface, there was neither ulceration of the surface nor any infiltration of the



and new acini may form (fig 10), the acinal epithelium may even become columnar in rare cases. The colloid never loses its staining characters, nor is there ever any papillation. In other words, these never take on the characteristics of exophthalmic goiter secondarily. Together with these acinal changes, the connective tissue always shows the foregoing peculiar changes, so that there still remains some justification for calling these tumors mixed tumors.

In the second type, the cell columns develop and come to resemble an adenocarcinoma in form. This may occur as rapidly-forming acini (fig 13) or by forming long columns (fig 14). This is the type

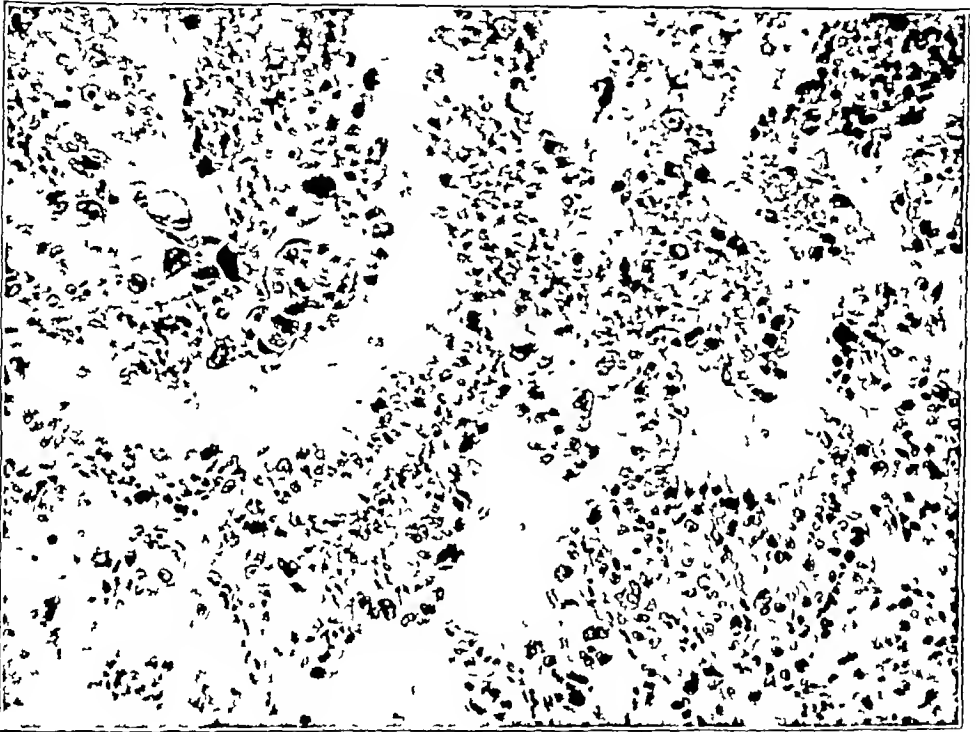


Fig 15—The acinal arrangement has been lost. A complete lobectomy removing all obvious tumor tissue failed to cure the patient.

that the laboratory worker is prone to diagnosticate as malignant. The type of connective tissue degeneration which forms a part of the life history of these tumors is strikingly like that seen in artificial tumors (produced by sudan III, tar, etc) and in the initial stages in roentgen-ray epitheliomas. It seems the part of wisdom to regard these tumors as at least potentially malignant when they show epithelial activity, and to govern the therapeutic activities accordingly. The mere fact that permanent cure follows their removal, in most instances before the capsule is invaded, does not invalidate this point of view. The fact remains that when distant metastases occur, this type of lesion is nearly always the cause. Most of the local malignancies are caused



the mode of growth of a benign tumor. The uniformity in the morphology of the tumor cells forming the alveoli which was found within the greater portion of the tumor was also a point in favor of its benign nature. The distinct morphologic variations in the appearance of the cells in the central portions of the tumor, the alteration of the nucleocytoplasm ratio, the hyperchromatic nuclei and the occasional mitotic figures, however, are features that speak in favor of malignant transformation.

The histologic opinion, therefore, was that of a benign adenoma originating from the epithelium of the excretory ducts of the bronchial mucous glands, but containing portions that exhibited a precipitate proliferation with signs of immaturity and anaplasia.

## COMMENT

The case reported here is that of a woman, aged 47, who had suffered for several years from symptoms of a respiratory disease associated with cough and expectoration, and had been repeatedly operated on for empyema in the right side of the chest. Since the symptoms continued she was admitted to the hospital where a cavity in the base of the right lung was found. An operation which was attempted to bring about the collapse of the cavity had to be discontinued on account of a profuse hemorrhage from the wound. After a short period of apparent improvement, another profuse hemorrhage from the wound was followed by almost immediate death. Autopsy revealed a polypoid growth springing off the wall of the main bronchus of the lower lobe of the right lung grossly showing definite benign characteristics, histologically an adenoma with features that make a malignant transformation in the center of the tumor probable. Numerous sacculated bronchiectatic cavities were present within the lower lobe of the right lung distal to the seat of the tumor, one of which opened directly on the surface of the lung and showed a communication with the sinus in the thoracic wall. An erosion of a branch of the pulmonary artery was found within one of the bronchiectases with a terminal hemorrhage from that vessel.

In correlating the postmortem observations with the clinical course of the disease, it appears evident that the symptoms were due to the extensive bronchiectases in the lower lobe of the right lung. The condition diagnosed as empyema was probably the result of the extension of the suppurative process from the bronchiectases into the pleural space, particularly, the cavity opening directly on the surface of the lung can be looked on as a continuous source of maintaining the suppurative process in the thoracic cavity. The final cause of death was the profuse terminal hemorrhage from the eroded branch of the pulmonary artery. It can be said, therefore, that the occluding polypoid tumor in the bronchus of the lower lobe of the right lung which caused the development of the bronchiectases (the mechanism of which will be discussed later) was undoubtedly responsible for the entire course of illness as well as for the final cause of death. The protracted course of the disease,

by these tumors. Like the mixed tumors of the salivary glands, these tumors tend ultimately to become malignant. It is only when this fact is recognized that one learns to appreciate the inherent tendency of these tumors.

#### COMMENT

It is important to emphasize that the tumors are not influenced by medication. This is easy enough to understand when it is remembered that the acini contain little if any colloid. While medication may influence the character of the cells after a prolonged period by causing change in the colloid, it cannot influence the connective tissue framework. This fact seems to have been overlooked by recent students of the influence of compound solution of iodine on toxic glands. Therefore, when one of these nodules is encountered, it should be removed or ignored. The patient may be assured that the removal of the tumor will be necessary some time. The objection to the removal of the tumors in young persons is that a true goiter may develop in later years which will be looked on by the patient as a recurrence. In such cases, it is well to acquaint the patient with this possibility. If treatment is being given for an early colloid goiter which harbors one of the mixed tumors, it is well to tell the patient that while the goiter as a whole will disappear, the nodule will remain unchanged though it may be less conspicuous by virtue of greater space being provided by the regression of the goiter.

Patients with mixed tumors may be assured that when these tumors become toxic, the toxicity is not extreme and that eye signs are never produced. These facts may be told patients in the first half of life.

When middle age is approached, while the foregoing facts may be admitted, it must be emphasized that the danger of future degeneration, and particularly the development of malignancy, is ever present and that removal of the tumor is to be urgently recommended.

Furthermore, when these tumors attain considerable size, associated with secondary degeneration, hemorrhage into them occurs, this may result in pronounced inflammation of the capsule and the surrounding tissue and painful affliction. Such a hemorrhage is far more serious when the tumor is associated with a colloid goiter or when it is located in the thorax. In such cases, the sudden enlargement and pressure of the tumor may quickly suffocate the patient.

For these reasons, the mixed tumors of the thyroid gland should be looked on as true neoplasms and not as goiter. While the tumors are benign in the earlier stages and allow certain degrees of improvement in treatment, they will cause trouble and require removal in the end. In this they differ from cysts, adenomas, and other benign nodules of the thyroid, not like those of the salivary glands.

extending as it did for a period of several years, is consistent with the presence of a benign tumor. The malignant changes revealed by the histologic examination can be regarded as of late occurrence and without significance for the clinical picture and the final events.

#### REVIEW OF LITERATURE

A survey of the literature in regard to intrabronchial new growth of epithelial origin reveals only a few cases that show features similar to the case here reported. In the case of Mueller,<sup>1</sup> a definitely benign pedunculated adenoma with partial calcification was found in the main bronchus of the left lung causing a partial occlusion of the lumen. Numerous sacculated bronchiectatic cavities filled with purulent and fecid material were present distal to the seat of the tumor. This case was that of a young woman, aged 22, who had suffered for a period of eight years from profuse expectoration of bloody and fecid material. The origin of this tumor was attributed to proliferation of the bronchial mucous glands. Another case of an epithelial polypoid tumor, which was considered as a cylindrical cell carcinoma originating from aberrant epithelium was found by Kreglinger<sup>2</sup> in the main bronchus of the left lung giving rise to almost complete obstruction of the lumen and atelectasis of the lung. In this case there was a history of massive expectorations for a period of six years, and numerous bronchial dilations could be demonstrated at autopsy. In view of the course of the disease, it seems justifiable to assume that originally this tumor was benign. Kirch<sup>3</sup> reported a case of a polypoid tumor in the main bronchus of the left lung with diffuse sacculated dilations of the distal bronchi, the histologic opinion was that of an originally benign fibromatous polyp with late malignant proliferation and tendency to infiltrative growth. A polypoid tumor in the main bronchus of the right lung located in close proximity to the lower lobe branch with extensive bronchiectases in the lower lobe of the right lung, was observed by Fleck<sup>4</sup> Malkwitz<sup>5</sup> reported a case of a primary polypoid tumor in the main bronchus of the left lung. Both these cases, however, presented definite malignant features with infiltration of the bronchial wall, and in both cases the origin was attributed to congenitally aberrant epithelium. A true

- 1 Mueller, Heinrich. Zur Histologiegeschichte der Bronchiektasenveränderungen, Inaug. Diss., Halle 7/5 1882.
- 2 Kreglinger, G. Über ein primäres Bronchiektasizom, Frankfurter Ztschr. f. Pathol. 12 135 1913.
- 3 Kirch, Eugen. Über stenosierende Bronchiektasien mit konsekutiver Bronchiektasenbildung. Centralbl. f. allg. Pathol. u. pathol. Anat. 28 545, 1917.
- 4 Fleck, Willi. Über primäres polypöses Bronchiektasizom, Inaug. Diss., Bonn, 1916.
- 5 Malkwitz, Frieda. Beitrag zur Kenntnis polypöser Bronchiektasien, Frankf. Ztschr. f. Pathol. 26 189, 1922.

would, therefore, be expected that the cycle of pathologic changes would be the same, whether the disease process were limited to certain regions or spread diffusely through the gland as a whole. These localized areas would become enlarged in a similar manner as a result of hypertrophy and hyperplasia in the active phase, and as a result of involution with the deposition of colloid and fibrous tissue in the inactive phase. Thus the greater the number of the disease cycles, the larger these nodules would become. It is not clear why only certain localized areas of the parenchyma become hyperactive in some cases while in others the entire gland is involved. When the pathologic process has begun the active phases (hypertrophy and hyperplasia) and the inactive phase (involution) of the disease cycle are attended by their characteristic histologic changes. It is possible that these localized areas of hyperfunctioning parenchyma originally may have been normal areas or lobules of the parenchyma of the gland which has undergone a pathologic hyperplasia, or, as suggested by Dr. Arnold Rich,<sup>3</sup> these areas may have originated in small isolated portions of the parenchyma commonly observed in the suprarenal and liver. In one part of his discussion on adenomas AlacCallum<sup>4</sup> says: "The thyroid adenomata are extremely common and here again it is sometimes difficult to feel sure that we are dealing with actual tumors and not with hypertrophy of the functioning gland." A similar opinion is expressed about the liver, suprarenal and other solid glandular organs. It is true that hypertrophy and hyperplasia of the thyroid gland may be encountered in conditions other than hyperthyroidism, such as the diffuse compensatory hypertrophy and hyperplasia seen in myxedema and in cretinism, and that produced experimentally in animals but we have never encountered a case of clinical hyperthyroidism in which hypertrophy and hyperplasia of the thyroid parenchyma could not be readily demonstrated. In the large hyperplastic nodular goiters of patients in whom the rate of basal metabolism is below normal and in whom the clinical picture is that of hypothyroidism, it is often possible to find histologic evidence of hyperactivity in certain limited regions. These areas which show slight hypertrophy and hyperplasia, are usually insignificant and may represent more actively functioning parenchyma or even the entire gland. In contrast hypertrophy and hyperplasia of an otherwise inactive

3 Rich A R Personal communication to the author.  
4 AlacCallum W G The Pathology of the Thyroid Gland, 1927, p. 115.  
49 115 (Oct 2) 1927 AlacCallum W G

gland, the hypertrophy and hyperplasia being compensatory here also. These points are brought out to demonstrate that mere hypertrophy and hyperplasia in a thyroid gland are not diagnostic of a clinical hyperthyroidism, since the hypertrophy and hyperplasia may be of a compensatory nature, either diffuse as in cretinism or regional as in hyperinvoluted nodular thyroids or colloid goiters. The point which we wish to emphasize, however, is that, given hyperthyroidism clinically, one always finds hypertrophy and hyperplasia of the thyroid parenchyma regardless of whether the gland is clinically nodular or the process is diffuse. In view of the fact that the hypertrophy and hyperplasia of the gland which invariably accompany clinical hyperthyroidism cannot always be distinguished histologically from the hypertrophy and hyperplasia of a compensatory type, attempts to draw clinical deductions from microscopic sections may lead to incorrect conclusions in many instances. The clinical syndrome must be carefully studied with the pathologic manifestations. Of the nine cases (8 per cent of 109) in which true benign neoplasms occurred in the thyroid concomitantly with a diffuse hypertrophy and hyperplasia of the gland as a whole, it may be said that this probably represents the normal incidence of true benign neoplasms in cases of nodular goiter. It would seem unlikely that these true tumors played any rôle in the production of the hyperthyroidism, and so far as this study is concerned, no functional significance can be attributed to their presence.

#### SUMMARY

Studies of the involutional changes occurring in the thyroid glands of patients with exophthalmic goiter who were undergoing remission following treatment with iodine revealed striking similarities to the histologic picture encountered in nodular goiter. When analyzed in connection with the involutional bodies, the pathogenesis of nodular goiter in about 92 per cent of the cases becomes evident. It was shown that a clinically typical case of exophthalmic goiter associated with a diffuse, smooth enlargement of the thyroid gland due to hypertrophy and hyperplasia of the parenchyma can give rise to a nodular goiter as a result of involutional changes in the thyroid concomitant with an artificial or spontaneous remission. These nodules or involutional bodies are not neoplasms in any sense of the word, but are merely regressive sequelae of a previous hypertrophy and hyperplasia of the parenchyma. Their number and size depend on the number of remissions and exacerbations in that gland. They are the products of a diffuse hypertrophy and hyperplasia of the thyroid, and it is likely that similar involutional changes occur in the breast and ovary or in other glands of flux. Thirty-four per cent of the cases in this study belong to this group.

polypoid adenoma in the main bronchus of the middle lobe of the right lung with complete obstruction of the lumen and cylindrical bronchiectases of the distal bronchial ramifications has recently been described by Heine,<sup>6</sup> the origin of this tumor is not definitely stated, both the surface epithelium of the bronchus and the epithelium lining the excretory ducts of the bronchial mucous glands are considered as possibilities.

From the foregoing cases, it appears evident that bronchial dilatations were almost invariably encountered in these cases of occluding intrabronchial neoplasms. Indeed, since the thorough investigations of Biermer<sup>7</sup> on the pathogenesis of bronchial dilatations, it is well established that intrabronchial tumors occluding the lumen may give rise to development of extensive dilatations of the distal bronchial ramifications. According to Biermer, the disturbance of the respiratory mechanism leading to an increase in the expiratory intrabronchial pressure is the factor primarily responsible for the development of the bronchiectases. It is the valvelike action of the occluding growth that affects the expiration much sooner and to a greater extent than the inspiration, which may for a considerable length of time go on undisturbed. The persistent cough driving the air from the surrounding alveoli into the bronchi under forced pressure is again a factor which increases the expiratory intrabronchial tension and which places a strain on the bronchial wall and leads to a gradual weakening of the elastic tissue. The ground for the dilatation appears well prepared and since hypersecretion is usually present in these bronchi, the accumulation of the secretion soon causes inflammatory changes which damage still more the contractile and elastic elements of the bronchial wall, so that finally no force is left that would counteract the dilating factors. If this process goes on for a sufficient length of time the inflammation may spread to the parenchyma of the lung, and as a result of this the normal elasticity of the lung is diminished or lost. As the lung is then not able to follow sufficiently the expansion of the chest during inspiration, an increased traction is exerted on it by the increased inspiratory negative pressure. This ultimately may act as an extrabronchial factor favoring the dilation of the bronchi.

Biermer's conception of the mechanism and the pathogenesis of bronchiectases distal from the point of bronchial occlusion seems to be well illustrated by the type of tumors with which we are dealing here. The well circumscribed pedunculated tumor endowed with more or less mobility appears particularly fit to reproduce the mechanism with its valvelike action. This is especially true for the slow growing benign

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6 Heine, J. Ueber eine primäre gestielte Bronchialgeschwulst, *Verhandl der deutschen pathol Gesell* **22** 293, 1927.

7 Biermer. Zur Theorie und Anatomie der Bronchienerweiterung, *Virchows Arch f path anat* **19** 94, 1860, *ibid*, **19** 241, 1860.

plexus can be seen beneath the floor of the region through the trans-parent prevertebral fascia and do not in any way belong in this space (b) The Posterior Compartment or the Posterior Cervical Triangle. The posterior compartment is a triangle bounded posteriorly by the trapezius muscle, anteriorly by the sternocleidomastoid muscle, and inte-riorly by the clavicle. Its floor or posterior wall is made up of the prevertebral fascia, a continuation of the floor of the sternocleidomastoid region. The areolar lymph gland bearing tissue, which, for the most part, makes up the contents of this compartment comprises glands of the superior deep cervical chain as well as inferior deep cervical systems draining the axilla and mediastinum. The glands of these two deep

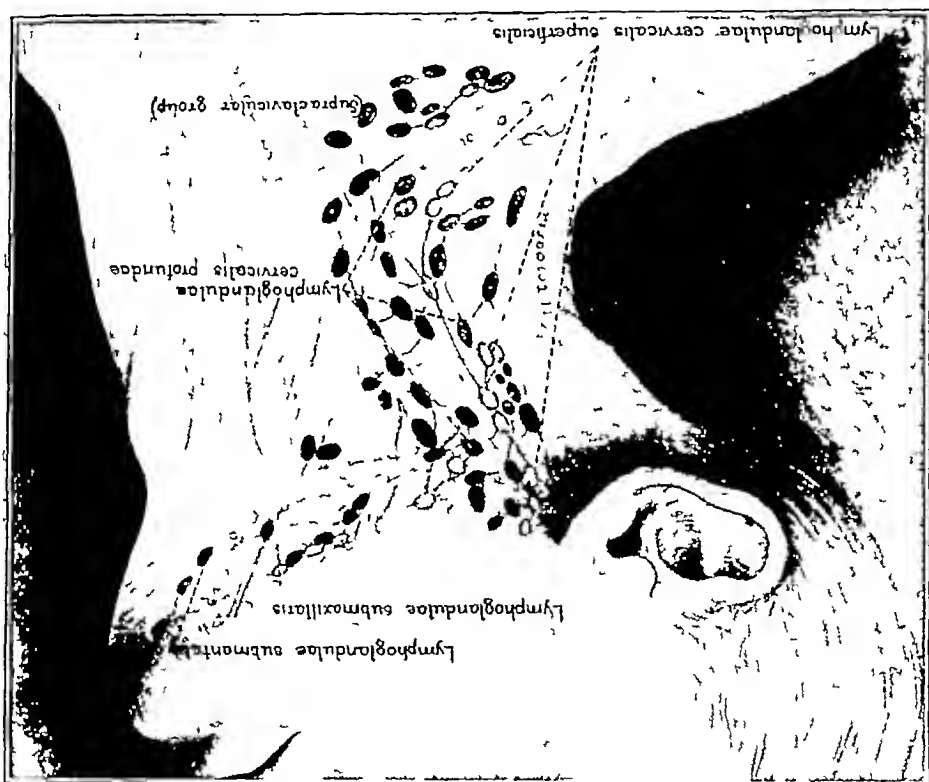


Fig 4—Schematic drawing to represent the distribution of the lymphatic gland chains of the neck and their relationship to one another and the neighboring structures. The deeper glands of the cervical chain are the ones primarily involved in carcinoma of the tongue. Note the close relationship between these glands and the internal jugular vein, the highest glands lying against the vein at the base of the skull and embedded in the lower pole of the parotid gland, the lowest gland at the lower edge of the omohyoid muscle as it crosses the vein, and the barren zone between this group and the suprahyoid chains constituting a break between the deep cervical glands and the supraclavical chains. The suprahyoid chains are primarily involved in carcinoma of the lip. The glands first affected are usually those lying against the ramus of the jaw along the edge of the sub-mandibular salivary gland and those at the apex of the submental triangle just beneath the point of the chin.

tumor without tendency to infiltration, but with a decided occluding growth which may exist for a considerable length of time as a silent tumor without causing symptoms of great significance. The cases in which only partial occlusion of the bronchus existed seem to illustrate this mechanism much clearer than the cases of complete bronchial obstruction. If a bronchus has been completely occluded at a relatively early period of the existence of the tumor, the possibilities for the development of bronchiectases become slight since the particular portion of the lung supplied by this bronchus loses its function completely and becomes atelectatic.

It is therefore the tendency to gradual occlusion of the lumen and the noninfiltrative growth that explains the fact that benign tumors in the bronchi are usually found associated with extensive bronchiectases. In addition to the foregoing cases of epithelial tumors there have been recorded several cases of benign occluding intrabronchial neoplasms of nonepithelial origin. A case is mentioned by Rokitsky<sup>8</sup> in which a lipoma in the main bronchus of the lower lobe of the left lung obstructed the lumen almost completely, the distal bronchial branches were dilated and the lower lobe of the left lung collapsed. Radestock<sup>9</sup> reported a rather unusual case of an obstructing tumor of the main bronchus of the right lung with numerous bronchial dilations and a cavity opening directly on the surface of the lung. Histologically, the tumor proved to be composed of thyroid tissue and its origin attributed to an aberrant thyroid. Siegert<sup>10</sup> reported a case of a chondroma within a branch of the bronchus of middle lobe of the right lung and Blecher<sup>11</sup> a case of a pedunculated ossified chondroma in the main bronchus of the left lung near the bifurcation, both of these cases presented numerous cylindrical bronchiectases distal from the seat of the tumor. A case of a pedunculated fibroma in the bronchus of the lower lobe of the right lung with cylindrical bronchiectases was described by Knack<sup>12</sup>. A lipomalike tumor in a branch of the bronchus of the middle lobe of the right lung was reported by Feller<sup>13</sup>.

8 Rokitsky, Carl. *Lehrbuch der pathologischen Anatomie*, 1861, vol 3, p 25

9 Radestock. Ein Fall von Struma intratrachealis, *Beitr z pathol Anat* 3 289, 1888

10 Siegert. Ueber primäre Geschwulste der unteren Luftwege, *Virchows Arch f path anat* 129 413, 1892

11 Blecher. Ueber die klinische Bedeutung der Bronchielekhondrosen, *Mitt a d Grenzgeb d Med Chir* 21 837, 1910

12 Knack. Ein Fall von Bronchiektasenbildung infolge eines Fibroms an der Abgangsstelle des unteren Hauptbronchus, *Deutsche med Wchnschr* 44 1007, 1918

13 Feller, Adolf. Ueber ein lipomähnliches Hamartom der Lunge, *Virchows Arch f path Anat* 236 470, 1922



cervical chains are separated by the posterior belly of the omohyoid muscle. The only important other structure in that area of the compartment superior to the omohyoid muscle is the spinal accessory nerve. This nerve runs a variable course from the posterior edge of the sternocleidomastoid muscle to the anterior border of the trapezius. The important structures in the area inferior to the omohyoid muscles are the subclavian artery and vein and several large branches of the axromi-thoracic trunk. Other vitally important structures of the neck are not occupants of this compartment, i. e., the cords of the brachial plexus as they emerge from the interval between the scalenus anticus and the scalenus medius muscle, the phrenic nerve, the inferior thyroid artery and the sympathetic chain, for these structures lie deep to the prevertebral fascia and, therefore, beneath the floor of the region.

#### SURGICAL DISSSECTION OF THE SUPRAPHYOID REGION

*Indication*—The suprahyoid dissection, independent of the dissection of the lateral region of the neck, is used for metastatic carcinoma of the hy when the indications for the complete dissection of the neck are lacking, that is, when gross examination of the submental and submandibular glands, at operation, do not show evidence of metastases. A complete or a combined dissection of the neck is necessary when there is gross involvement of the submandibular or submental groups. This follows from the general rule regarding metastatic carcinoma that secondarily chains must be removed where there is gross involvement of the primary chains. Seldom, however, does carcinoma of the hy require more than the simple operation on the suprahyoid region.

The uncombined, or the pure suprahyoid dissection of the neck is often a bilateral procedure, because usually the lesion of the hy crosses the midline or is near the midline. The bilateral dissection adds little to the operation and it gives the patient a symmetric neck. This procedure should follow the resection of the local primary lesion as soon as convenient, and always within a few weeks, providing the microscopic study of the primary lesion shows a growth of sufficient extent to have infiltrated the muscle of the hy or in any case regardless of the extent of the growth where there is a total lack of differentiation of cells (Broders).

*Method of Procedure*—A cut throat incision is employed (Fig. 25) extending from mastoid process to mastoid process and passing across the front part of the hy just above the hyoid bone. This incision is divided at a right angle at the mastoid process and then extends from the mastoid process only a short distance across the hy to the mastoid process. The opposite dissection is made on the other side of the hyoid bone. The superior hy is dissected up taking care to divide the hyoid bone. The tissue while the inferior hy is dissected. The inferior hy is dissected up and the insertion of the thyrohyoid muscle is noted.

Those rare cases of tumor development in cases of bronchiectases of long standing, such as those reported by Chiari,<sup>14</sup> must be regarded as a different entity. In a case of diffuse chronic tuberculosis of both lungs with occasional sacculated bronchiectases, he observed a tumor in one of the cavities which histologically proved to be a proliferating adenoma originating from the bronchial mucous glands. The other case of Chiari was that of a mixed tumor, a lipochondro-adenoma in an old sacculated bronchiectatic cavity. These tumors are to be considered as secondary to the bronchiectases being the sequel and not the cause of the latter. Such tumors, according to Chiari, may develop in the course of the dilatation of the bronchi in a similar manner as proliferation of the papillary type commonly found in old bronchiectases.

The fact that extensive bronchiectases are less frequently found in cases of malignant bronchial tumors is explained by their more rapid growth, the metastases and the general deleterious effect on the organism which usually cause death long before there is sufficient time to develop bronchiectases. The ulceration and the degenerative changes which these tumors frequently undergo may also be a factor in preventing a marked degree of bronchial occlusion. Occasionally, however, marked bronchiectases are seen in malignant neoplasms, particularly in the nodular or papillary form as in the cases of Biermer,<sup>7</sup> Muethler<sup>15</sup> and Reiche<sup>16</sup>.

We mentioned at the outset the importance of bronchoscopy as a valuable diagnostic aid in intrabronchial neoplasm. Reports in the literature indicate that there is also a therapeutic field for this method, particularly in cases of benign tumors. Spiess<sup>17</sup> removed a polypoid tumor of the main bronchus of the right lung lodged just at the bifurcation by means of the bronchoscope after tracheotomy had been performed. The patient who had suffered from severe dyspnea with attacks of suffocation showed marked improvement. An endothelioma of the main bronchus of the right lung was removed by Jackson<sup>18</sup> by means of peroral bronchoscopy and the patient observed for one and one-half years as free from symptoms. Pfeiffer<sup>19</sup> used the same method in

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14 Chiari. Zur Kenntnis der Bronchialgeschwulste, Prag med Wchnschr 8 497, 1883

15 Muethler, Gustav. Ein Fall von Bronchostenose durch ein Sarkom bedingt, Inaug. Dissertation, Berlin, 1873

16 Reiche, F. Primäres Tracheakarzinom, Metastase in der linken Nebenniere, Melasma suprarenale, Centralbl f allg Pathol u pathol Anat 4 1, 1893

17 Spiess, Gustav. Ein Fall von hochgradiger Dyspnoe infolge eines Polypen im rechten Bronchus, Munchen med Wchnschr no 40, p 2095, 1910

18 Jackson, Chevalier. Endothelioma of the Right Bronchus Removed by Peroral Bronchoscopy, Am J Med Sc 153 371 (March) 1917

19 Pfeiffer, Willy. Das Jacobson-Holzknicht'sche Phänomen bei einseitiger Bronchostenose und seine künstliche Erzeugung, Deutsche med Wchnschr no 47, p 1298, 1920

This lays bare the contents of the triangles to be dissected, covered by the enveloping fascia. With a sharp blade this fascia is divided all along the anterior border of the mandible and over the parotid gland from chin to sternocleidomastoid muscle. By a "wiping down" process or blunt dissection, the separation of the glandular and areolar contents from the periosteum of the bone, from the parotid gland, and from the outer surface of the mylohyoid and hyoglossus muscles is accomplished. This cleaning-out process is early held up by the facial vessels, which must be ligated and cut where they pass over the horizontal ramus of the jaw (fig 6). At this point, one proceeds with caution until the marginal branch of the mandibular nerve (seventh) is isolated and retracted out of danger. This nerve can be located best and traced out by picking it up as it comes across the ramus of the jaw together with the facial vessels (*Maxillaris externa*). The destruction of this nerve means a permanent paralysis of the lower angle of the mouth. The "wiping down" process may now continue with the cleaning off of the outer surfaces of the

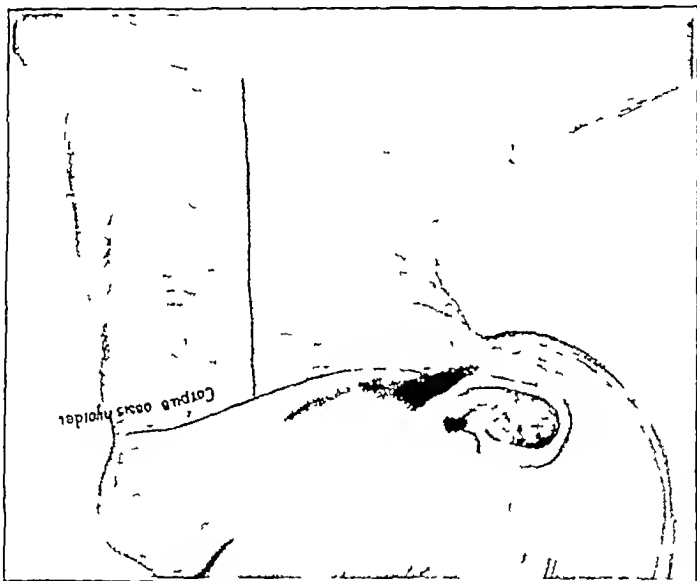


Fig 5—Incisions employed for dissections of the neck. The horizontal line represents the incision for suprahyoid unilateral dissection. It extends from the mastoid to the anterior belly of the digastricus of the opposite side. It lies in a natural fold of the neck and passes just above the hyoid bone. Deviation from this line should not be made regardless of possible wrinkles, as this always gives the best cosmetic result. The upper flap only is lifted. The vertical line represents the incision for the lateral dissection. It extends from the middle of the horizontal incision and strikes the clavicle just lateral to the sternocleidomastoid muscle at its insertion on that bone.

mylohyoid and hyoglossus muscle. It is again halted by the submaxillary branch of the lingual nerve, by the submaxillary duct and by the plexus of veins about the duct. The submaxillary branch of the lingual nerve enters the superior pole of the salivary gland, accordingly, traction downward of this gland, along with the areolar and lymph glandular contents of the triangle, pulls the lingual nerve into view (fig 7). The junction point of the nerve branch with the lingual nerve is situated just beneath the lateral border of the mylohyoid muscle near its upper edge. Retraction medially of the lateral border of the muscle is

removing a fibroma from the main bronchus of the left lung and has seen the patient well seven years after the operation. Another case of fibroma in the main bronchus of the left lung is mentioned by Wessler and Jaches,<sup>20</sup> on roentgen-ray examination this case showed an almost complete atelectasis of the left lung, which after bronchoscopic removal of the tumor cleared up rapidly. Recently Orton<sup>21</sup> reported a bronchoscopic removal of a pedunculated growth from the bronchus of the middle lobe of the right lung, although in this case the histologic opinion was in favor of a malignant tumor, the patient was well four years after the removal of the growth.

We have seen that intrabronchial tumors, while being benign both in their gross appearance and histologically, may lead to rather serious and even grave consequences due to their particular location. An early diagnosis and operative procedure, especially removal by means of bronchoscopy may often prevent extensive pathologic changes and be of great benefit for the patient.

#### SUMMARY

1 A case of a polypoid adenoma of a large bronchus originating from the excretory duct of the bronchial mucous glands is described.

2 The mechanism of the consecutive formation of bronchiectases is discussed.

3 The literature on the subject is reviewed.

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20 Wessler and Jaches. *Clinical Roentgenology of Diseases of the Chest*, Troy, N. Y., 1923, p. 51.

21 Orton, Henry Boylan. *Carcinoma of the Bronchus*, *S. Clin. N. Amer.* 6: 1534, 1927.

usually necessary for exposure. Division of this salivary branch frees the gland and allows the lingual nerve to retract out of danger. The salivary duct is exposed where it enters the base of the tongue by strong traction medially and on the lateral edge of the mylohyoid muscle. Ligations and divisions of the duct and veins release the last hold on the triangle contents. Again caution needs to be observed because the hypoglossal nerve traverses the triangle near the salivary duct and sometimes in the midst of the mass of veins. Before ligation of these veins in this angle, therefore, the nerve should be identified and pushed aside. The dissection is now completed without further interruptions by the final clearing off of the mylohyoid and the hyoglossus muscles down to the posterior belly of the digastricus and the styloid muscle and the central

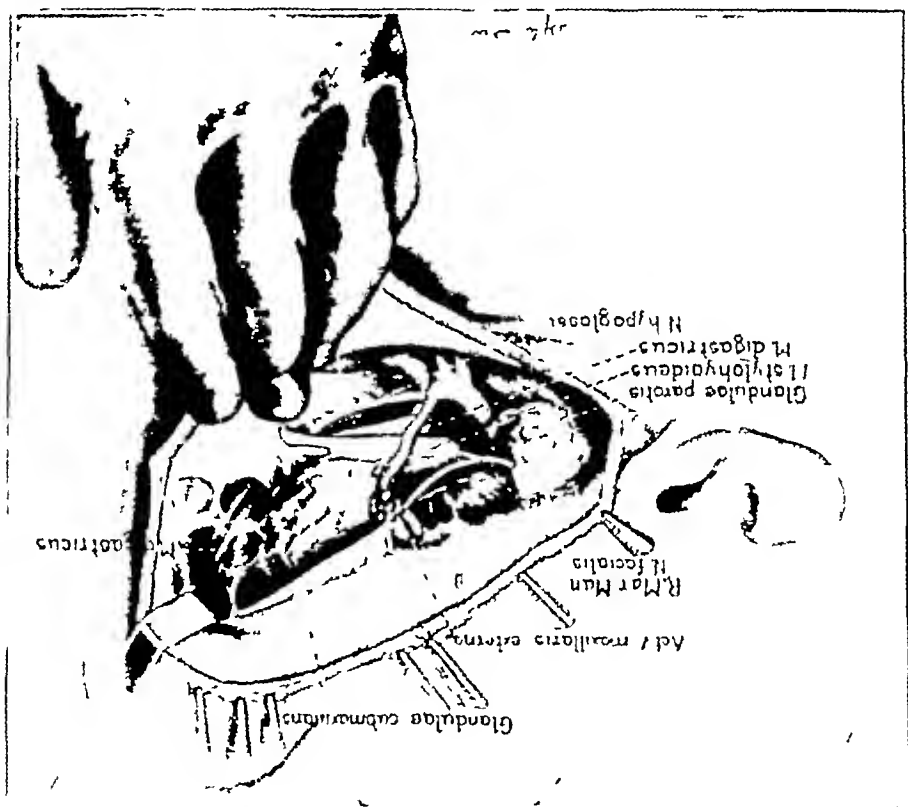


Fig. 5.—Early stage suprathyroid dissection. The facial vessel have been divided; the marginal branch of the mandibular (seventh) has been isolated and preserved. The branch of this nerve to the platysma muscle and the thyrod and is so pictured. The lower pole of the parotid gland has been cleaned out and is still intact. The submaxillary salivary gland has been freed from the ramus of the jaw by the sharp division of the cervical artery. The drawing is of a true representation of the actual dissection in that the submental triangle is shown, and the lower lip has been lifted to show structures below the level of the lower lip. The submental triangle is copied in all dissection of the triangle. The lower lip in the pure suprathyroid dissection is not cut behind.

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# DISSECTIONS OF THE NECK \*

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Observations of the too frequent indifferent methods and the correspondingly poor results obtained in dissections of the neck in general, invite an attempt to develop an orderly and clearcut technic and a definite understanding of the objects to be attained. The substance of this paper recalls the teaching of the surgical masters of the past and present and, in addition, records the experiences of the authors throughout a decade of surgical operations of the neck.

## CLINICAL INDICATIONS

Dissections of the neck are performed for metastatic carcinomas, primary endotheliomas, localized Hodgkin's disease, intractable tuberculosis and for less frequent conditions, such as lymphosarcoma, carcinoma of the brachial cleft and tumors of the carotid body. Our purpose is to outline a method for the eradication of malignant processes which are primary elsewhere and metastatic in the neck. Primary carcinoma of the lower lip or of the skin of the face below the mouth metastasizes to the glands immediately inferior to the mandible, while carcinoma of the cheek, tongue, tonsil, pharynx, antrum and the lateral portions of the face, metastasize primarily to the lateral regions of the neck. Accordingly, from the surgical metastatic standpoint, the neck is divided into two metastatic regions, i e, the suprahyoid region for carcinoma about the lip and the lateral region of the neck for the other growths enumerated.

## ANATOMIC CONSIDERATIONS

The structures of the neck are so complex and the surgical procedure is so fraught with dangers in the hands of the uninformed, that a thorough anatomic understanding of the neck is of first importance.

*A Suprahyoid Region of the Neck*—The suprahyoid region (fig 1) or, in general, that region between the mandible or lower jaw and the hyoid bone, is divisible into three compartments: a submental compartment and two submaxillary compartments.

The submental division of the suprahyoid region is a triangle bounded laterally by the anterior bellies of the digastric muscles and inferiorly by the hyoid bone. The apex of this isosceles triangle is at the symphysis of the mandible. The anterior wall or covering of the submental

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The contents of the submental region, while removed separate from those of the submaxillary compartment, are, in reality, continuous with those of the submaxillary and lie on a common floor. The anterior belly of the digastric muscle, therefore, must be lifted so as to thoroughly clean the mylohyoid floor. The parotid gland is not disturbed in this dissection.

SURGICAL DISSSECTION OF THE LATERAL REGION OF THE NECK

*Indications*—Dissection of the lateral region of the neck is sometimes carried out just as subsequently described, but usually it is combined with and follows the suprahyoid dissection. The combined suprahyoid and lateral operation, with or without modifications, is performed for metastatic carcinoma of the buccal cavity, for primary carcinoma of

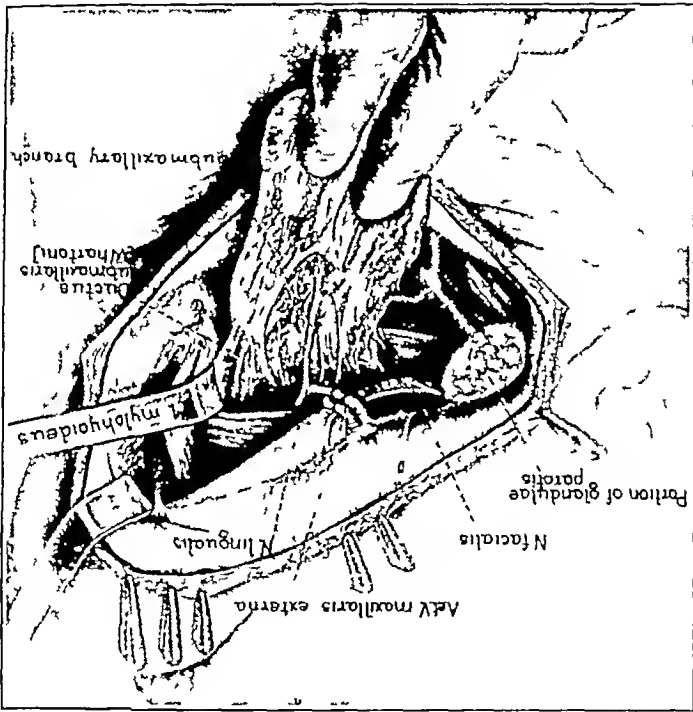


Fig 7—A late stage in the suprahyoid dissection. The lingual nerve has been pulled down into view. It will retract out of danger when the branch to the submaxillary salivary gland has been divided. The hypoglossal nerve crosses the angle made by the two bellies of the digastric muscles just beneath the duct on the hyoglossus muscle floor at the point represented by the star.

the branchial cleft, with or without metastases for primary endothelioma arising in the lymph glands of the neck, for Hodgkin disease and occasionally, for severe cervical tuberculosis. It is carried out without modifications in all instances of metastatic carcinoma and must be performed in all cases of primary carcinoma within the buccal cavity regardless of metastasis. This holds true regardless of the size of the lesion or the extent of the infiltration with the possible exception of

compartment is made up of the skin and the platysma muscle as well as a sheet of enveloping or deep fascia of the neck. Its posterior wall or floor is composed of the anterior portions of both mylohyoid muscles. The contents of this compartment are simply loose areolar tissue containing lymph glands without important nerves or blood vessels.

Each submaxillary region is also a triangle bounded laterally and below by the two bellies of the digastric muscle and above by the horizontal ramus of the mandible prolonged to the parotid gland. It is covered by the skin and platysma, deep to which is attached a thin layer

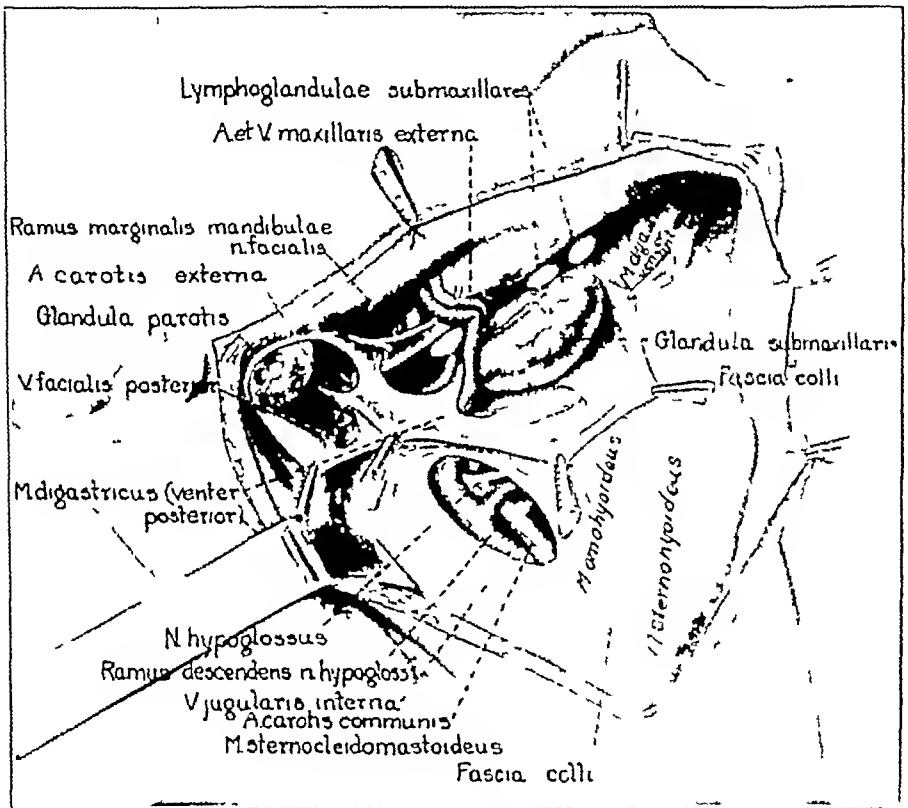


Fig 1—Dissection to show the submaxillary compartment. The skin-platysma flaps expose the enveloping fascia of the neck which has been partly removed to show the contents of the compartment and its investment of the parotid gland together with its relation to the great vessels.

of enveloping aponeurosis continuous with that over the submental triangle. The floor or back wall is composed of the lateral portions of the mylohyoid muscle and the underlying hyoglossus muscle projected laterally to the anterior border of the sternocleidomastoid muscle and the parotid gland.

The contents of the compartment are more important than those of the submental triangle. Each contains a submaxillary salivary gland, the facial vessels, a quantity of loose areolar tissue in which are



occasional instances of early and strictly localized carcinoma of the cheek or of the gums. Dissection of the neck may precede or follow, or may be combined with the operation on the local lesion. Usually it should precede this operation so as to block off the local area to be treated.

*Method of Procedure*—The incision for the combined suprathyoid and lateral dissection is T-shaped, the horizontal incision being simply that already described for the unilateral suprathyoid dissection (fig 5). The vertical incision is dropped from the midpoint of this horizontal line and strikes the clavicle near the lateral edge of the sternocleidomastoid muscle. This same incision is employed where the lateral dissection alone is to be made.

The two lateral flaps consisting of skin, fat and platysma are turned back, the posterior as far as the anterior edge of the trapezius muscle and the anterior so as to expose the ribbon muscle of the thyrod (fig 8). The area to be cleared out is then outlined posteriorly by the division of the enveloping fascia along the anterior edge of the trapezius muscle and the clearing away of the areolar tissue in this plane down to the prevertebral fascia covering the floor of the neck. This exposes the spinal accessory nerve and divides many sensory branches of the cervical plexus. The area is outlined medially by the division of the enveloping and pretracheal fascia just lateral to the ribbon muscles of the thyrod, with the consequent exposure of the common carotid artery (fig 8). The inferior limits of the area to be dissected are worked out as follows. The sternocleidomastoid muscle is cut transversely about 5 cm above the clavicle, or approximately at the level of the crossing of the omohyoid muscle. The clavicular stump of this muscle is cleaned off on its inner surface and turned back down over the clavicle. It is used later to fill the dead space in the suprathyoid fossa. By blunt and sharp dissection, the suprathyoid tissue is now divided along a straight line paralleling and about 3 cm above the clavicle or at a level approximately 2 cm below the omohyoid where it crosses the deep vessels. This line must be below the numerous middle portion of the omohyoid in order to include the whole of the deep cervical chain of lymph glands because the lower end of this chain lies just below the omohyoid over the lateral wall of the internal jugular vein (fig 4). It need not be placed lower than this line because the lymph glands about the subclavian vessels need not be removed even when the lower deep cervical gland is grossly involved, chemical experiments having shown that the subclavian chain is rarely involved in metastases or malignant extension of the neck even when that condition is advanced. Also at this level the operation is more simple, owing to the fact that there is no danger of wounding the subclavian vessels. As the tissues are divided the most important structures of the external jugular vein, which is ligated and divided at the lateral corner. Almost at the same depth in the medial angle the internal jugular vein is exposed. This vessel is also picked up doubly ligated and divided. The dissection is carried down to the floor of the neck, that is, to the prevertebral fascia overlying the deep muscles. Many small vessels must be ligated in this area, but not but no structures of any vital importance are encountered.

With the accomplishment of this initial dissection the suprathyoid and lateral dissection is now ready to be carried out. The suprathyoid dissection is now carried out in the usual manner, the suprathyoid muscle being removed and the suprathyoid fossa being filled with the suprathyoid muscle.

embedded several lymph glands, and the more vital structures, namely, the hypoglossal and the lingual nerves. The facial vessels traverse the compartment in its lateral halt and cross over the horizontal ramus of the mandible at a point approximately midway between the angle and the symphysis. The hypoglossal nerve crosses the compartment near its inferior angle where the digastric bellies attach themselves to the hyoid bone. It lies deep to the mylohyoid muscle, and its further course over the hyoglossus is in the cleft between the two muscles. The lingual nerve lies hidden by the ramus of the jaw and courses along and in the sulcus between the under surface of the mandible and the floor of the hyoglossus. Perhaps the largest branch leaves the nerve at the posterior margin of the mylohyoid and immediately enters the substance of the submaxillary gland.

Two important near-related structures which do not actually lie within the compartment are the marginal mandibular branch of the facial nerve and the inferior pole of the parotid salivary gland. The marginal mandibular nerve courses along the outer surface of the mandible, deep to the platysma, but superficial to the enveloping fascia. The inferior pole of the parotid gland is separated from the true compartment by only a thin fascia and is thoroughly exposed in both anatomic and clinical dissections.

*B Lateral Region of the Neck*—Under the heading of the lateral region (figs 2 and 3) of the neck we include all the structures between the trapezius muscle laterally and the ribbon muscles of the thyroid gland mesially, the clavicle inferiorly, and the posterior belly of the digastric muscle with the base of the skull superiorly. This region so described includes, therefore, the rest of the neck, only those structures which are strictly infrahyoid being omitted, i. e., the thyroid gland, the laryngo-tracheal tube and the esophagus.

The roof or outer covering of this general region is made up of the skin platysma layer and the enveloping layer of the deep fascia of the neck. The posterior wall or floor is the prevertebral fascia covering the deep muscles of the neck. This space is naturally divided into subcompartments, i. e., a region overlaid by the sternocleidomastoid muscle, the sternocleidomastoid or carotid region, and the region posterior to it, the posterior cervical triangle.

(a) *The Carotid or Sternocleidomastoid Region*. This region is an elongated quadrilateral space, bounded by the borders of the sternocleidomastoid muscle, by the mastoid process and the clavicle. In depth, it is considered to extend to the prevertebral fascia.

The sternocleidomastoid muscle, invested by the splitting of the aforementioned enveloping fascia which helps form the roof of the entire neck, may be said to overlie the region at hand. In consideration of this muscle, it should be here noted that the spinal accessory nerve

internal jugular vein (fig 9) In this step the common carotid artery, the vagus nerve and the prevertebral fascia are thoroughly cleaned of loose areolar tissue The upward dissection may be carried out without fear of mishap or danger to any vital structures because the vagus nerve and common carotid artery are always plainly visible, and the brachial plexus and phrenic nerve are protected by the prevertebral fascia This fascia, which is never disturbed, is identified as a transparent tough covering closely adherent to the deep muscles of the neck All branches of the cervical plexus come out through this fascia

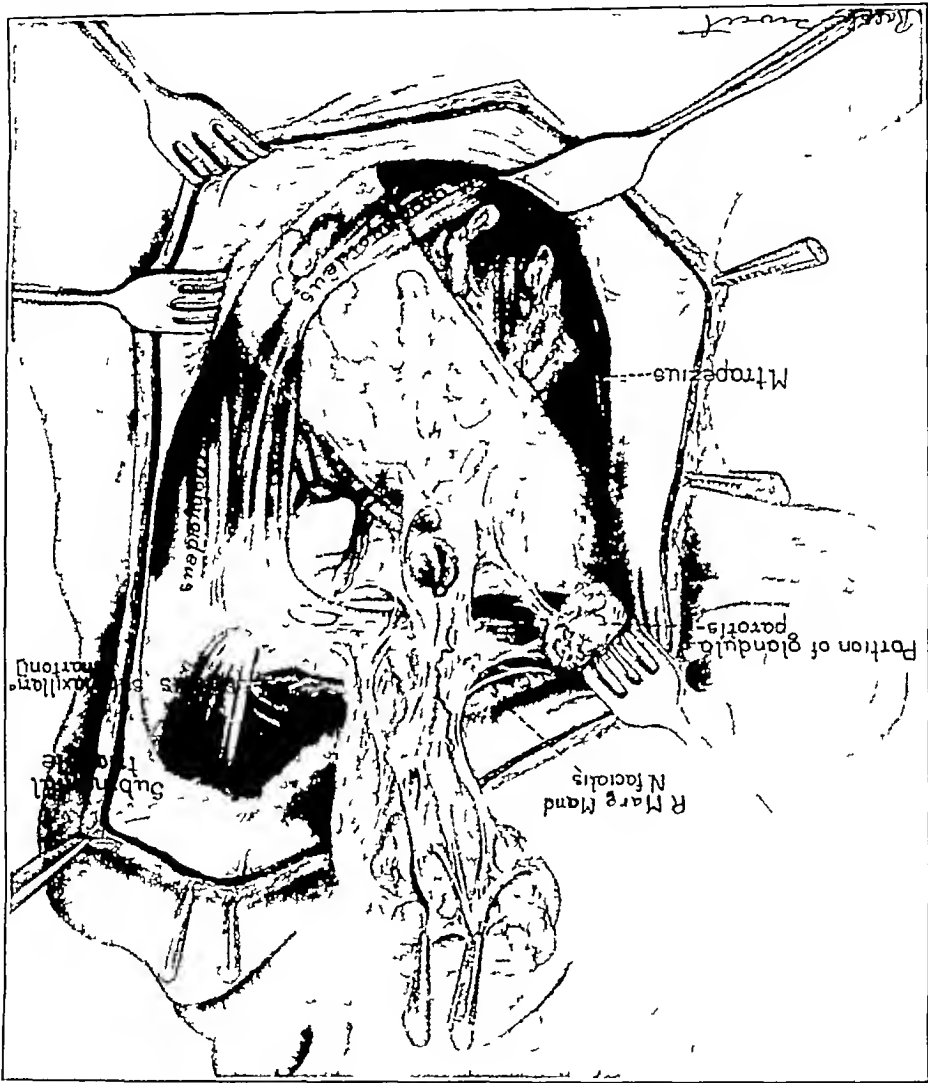
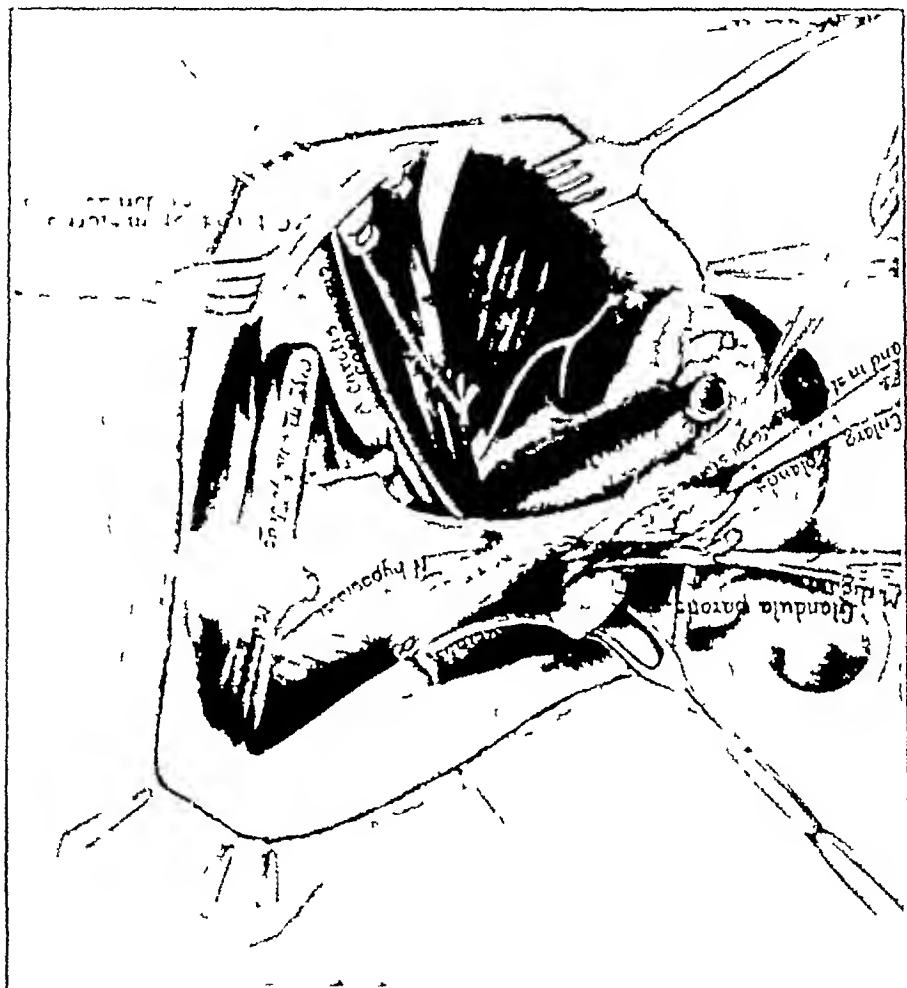


Fig 8—Early stage of the complete dissection of the neck The suprahyoid dissection has been completed down to the upper margin of the posterior belly of the digastricus The lateral flaps of skin and platysma have been dissected back The edge of the trapezius marks the lateral limits and the thyroid muscles mark the medial limits of the area to be dissected The lower limits are defined by dividing the omohyoid and sternocleidomastoid muscles at the level of the crossing of the lower edge of the omohyoid and the lateral edge of the sternocleidomastoid



Fig. 9.—Later stage of complete dissection of the neck. The area to be dissected has been outlined below by the division of the sternocleidomastoid muscle; the ligature and division of the external jugular veins, and the separation of the deeper tissues down to the prevertebral process of clearing on the heart the carotid artery, lymphatic vessels, and stripped of all loose tissue. The branches of the carotid, jugular, and subclavian have been cut through the government of the prevertebral ganglia. The body of the pharynx in the neck is covered by the prevertebral fascia, and is situated between the carotid vessels and the subclavian vessels.



except the phrenic nerve, and all, with this one exception are divided at their point of emergence, through the fascia. No branches of the carotid artery will be seen until the bifurcation which takes place at about the level of the most prominent part of the "Adam's apple." Usually the first indication that the point of bifurcation has been reached is the finding of a branch, the superior thyroid, apparently coming off from the common carotid vessel. This is due to the fact that the internal carotid lies behind the external at the bifurcation and both are enclosed with a common sheath for one or more centimeters. The bifurcation can always be demonstrated, however, as taking place proximal to this

The lymph glands are largely those of the superior deep cervical chain, and they lie mainly in the loose areolar tissue about the vessels in the upper two thirds of the region. A few glands of this chain extend a little below the junction of the two bellies of the omohyoid muscle, and a few supraclavicular glands of the subclavian or inferior deep cervical chain lie along the upper margin of the clavicle. There is continuity between the superior deep cervical chain of glands and

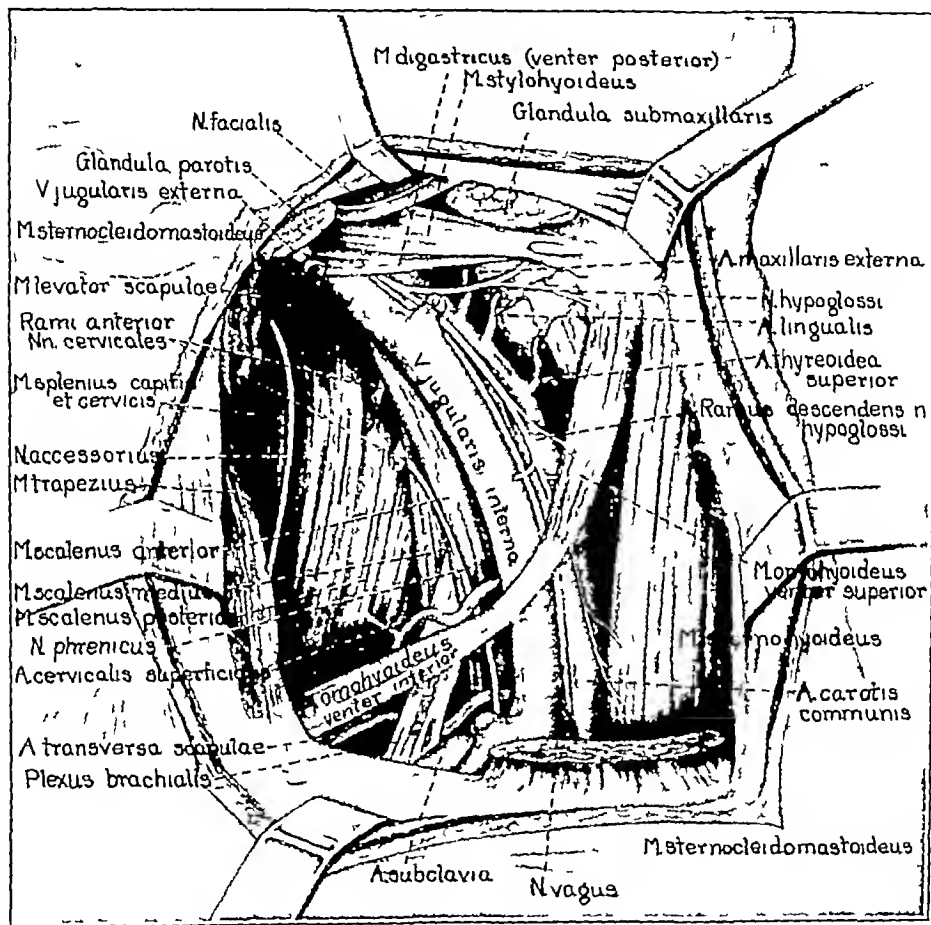


Fig 3—The lateral region of the neck. The sternocleidomastoid muscle is removed to show the structures deep to it and the continuity of the carotid and the posterior cervical divisions of the region.

the submaxillary glands superiorly and with the inferior deep cervical or supraclavicular glands inferiorly.

The contents of the carotid sheath are the common carotid artery, the internal jugular vein and the vagus nerve. The common carotid artery runs from below upward under cover of the mesial border of the sternocleidomastoid muscle as far as the upper margin of the thyroid cartilage, where it bifurcates into its internal and external jugular branches. Over the course of the common carotid artery the internal jugular vein

branch. As soon as the identification is clear, a ligature is shipped about the external carotid artery and tied just proximal to the superior hyoid branch, thus insuring the ligature from slipping off the end. Both vessels are then divided after clamping or ligating the distal stumps. The upward dissection should now proceed smoothly providing the medial area is dissected first until the tendinous portions of the stylohyoid and digastricus muscles and the hypoglossal nerve are exposed. Great care must be taken to isolate the hypoglossal nerve which makes a loop below the level of the posterior belly of the digastricus muscles, extending frequently 2 cm below the lower border at the central portion of the belly and crossing under the muscle in its tendinous portion at the hyoid cornu (fig 9). The nerve is easily identified rather deep on the floor of the neck, if sought for beneath the hyoid cornu. Dissection may now continue upward and lateralward following the stylohyoid muscle in the direction of the styloid process, and is usually carried through to the base of the skull. Frequently, however, it is not possible to proceed further than the isolation of the hypoglossal nerve because of metastatic masses which prevent the proper turning up of the contents of the neck and the complete exposure of the floor of the neck at the base of the skull. Working in this corner without sufficient room may result in the nicking of the internal jugular vein on its under surface with an obscuring of the field and discoloring of the tissues from flooding of the area with venous blood.

The last step takes place at the upper lateral angle, and has to do with the cutting away of the sternocleidomastoid muscle from the mastoid process, with the taking away of the lower pole of the parotid gland, and the ligation of the internal jugular vein at the skull (fig 10). The lower part of the parotid gland (approximately from 1 to 2 cm) must be taken because some of the lymph glands at the upper end of the deep cervical chain lie embedded within this structure. In cutting through the parotid, innumerable veins, many of considerable size, must be divided, and progress here usually is slow. On completing this dissection the most difficult task still remains, i.e., the isolation and ligation of the internal jugular vein and the identification and preservation of the vagus, the hypoglossal and the spinal accessory nerves. These nerves lie close to the floor of the neck, also close to the vein, so that mass ligature is not possible. It is well to approach the vein from one side and then the other, leaving the direct working down on the vessel as the last step. The complete removal of the internal jugular vein is required because of two facts, namely, the intimate relationship of the lymphatic vessels and glands with the sheath of the vein all along its course and the location of the highest gland in the deep cervical chain against the vein at the skull (fig 4). The spinal accessory nerve too often must be sacrificed in the radical dissection for carcinoma, because in its passage through the sternocleidomastoid muscle it frequently becomes involved in a tumor mass and cannot be separated without danger of leaving carcinomatous tissue behind.

With the completion of the dissection, the floor of the neck is clear, that is, the prevertebral fascia has been cleaned of all loose areolar tissue and is everywhere intact. The vagus, hypoglossal, and frequently, the spinal accessory cranial nerves may be seen lying on the floor of the neck, the vagus lying against the lateral wall of the common carotid artery, the hypoglossal looping down beneath the posterior belly of the digastricus muscle and disappearing underneath its end at the hyoid bone, and the spinal accessory passing obliquely downward and backward to disappear beneath the edge of the trapezius near the lower angle of the wound at the lateral corner. The common and internal carotid arteries are

lies external to it. Superior to its bifurcation however the internal carotid artery runs posterior to the internal jugular vein in its course to the base of the skull. There are no branches to the internal or the common carotid artery in the neck while the external carotid in our region gives off the superior thyroid, lingual and external maxillary branches. The superior thyroid artery leaves the parent trunk about 1 cm. from the bifurcation and the lingual and facial vessels at a more distant point.

The internal jugular vein begins at the base of the skull deep and anterior to the mastoid process of the temporal bone and deep to the external auditory meatus. It passes downward and forward beneath the sternocleidomastoid muscle and lateral to the common carotid artery.

The vagus nerve leaves the skull beside the internal jugular vein and courses mesial to this vein as far as the common carotid artery, where it lies between and behind these structures in the carotid sheath until its entrance into the mediastinum.

The hypoglossal nerve emerges from the base of the skull near the two foregoing structures and courses with them for a short distance to a point on a level with the hyoid bone, so that it runs forward and upward and crosses between the posterior belly of the digastric muscle and the hyoglossus muscle to the submaxillary compartment as has been already described. The spinal accessory nerve leaves the skull soon to traverse the superior third of the sternocleidomastoid muscle and to be distributed through the posterior compartment to the trapezius muscle.

The veins from the face, the tongue and the thyroid gland enter into a more or less common trunk, the thyrolingual-facial trunk, which lies in the superior portion of the region and communicates with the internal and external jugular vein.

The anterior branches of the cervical plexus with the exception of the phrenic nerve, pierce the prevertebral fascia to emerge through the posterior triangle at about the posterior margin of the sternocleidomastoid muscle. There are the great auricular and the lesser occipital nerves and, in general, the nerves that supply the scapula. The phrenic nerve lies on the anterior scalene muscle deep to the prevertebral fascia or the floor of the region.

The parotid gland while encased in a compartment of its own is nevertheless in intimate relation not only with the submaxillary region but with the superior portion of the sternocleidomastoid region. Its importance in this discussion lies in the fact that some of the lymph glands of the superior deep cervical chain are in close contact with its interior pole.

Within the region on the left side the thoracic duct enters this compartment from the chest and empties into the junction of the left subclavian and the left internal jugular vein. The cords of the brachio-



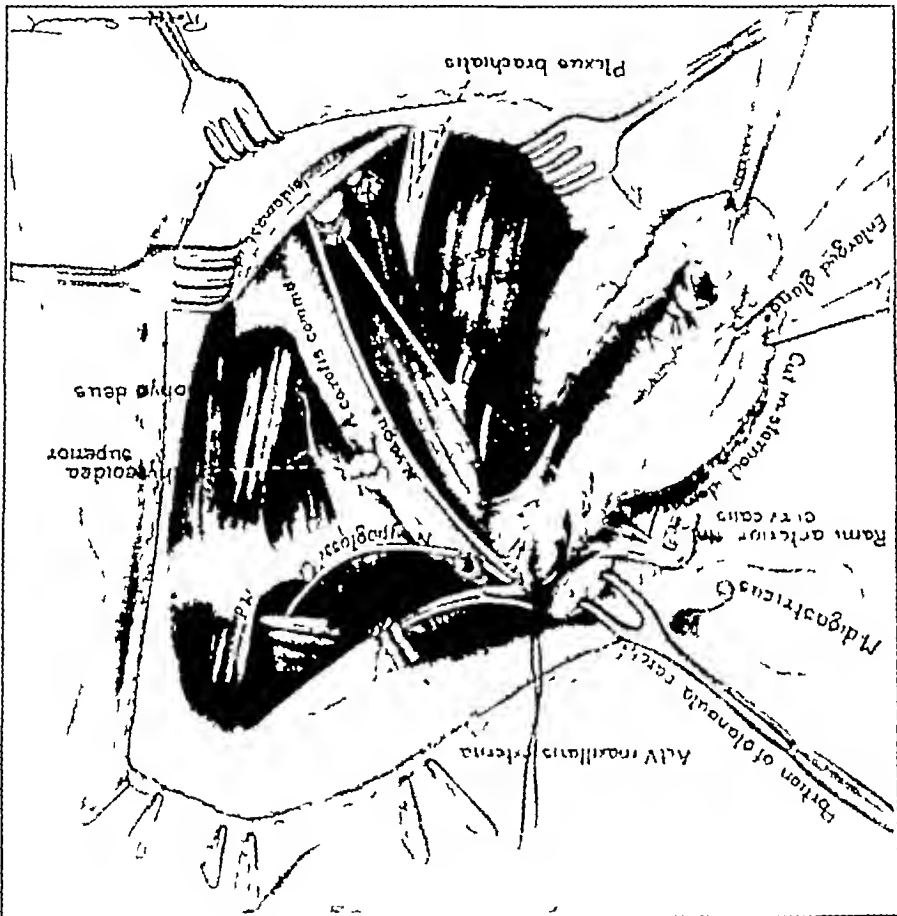
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Fig 10—Last stages of complete dissection of the neck. The external carotid artery has been doubly ligated and divided. The hypoglossal nerve has been stripped and carefully preserved. The lower pole of the parotid gland has been taken away and the jugular vein has been ligated at the base of the skull. This cannot be shown accurately because the point of ligation would be too high up under the parotid and angle of the jaw to be visible from this angle. The vagus, hypoglossal and accessory nerves lie close to the vein at the site of ligation and must be identified before the ligature is placed.

medial angle alongside and lateral to the common carotid artery. The remaining mass of loose areolar tissue surrounding the subclavian vein and covering the apex of the lung, pumps up and down with respiration.

In sixty-three cases (68 per cent) the thyroid gland was not involved diffusely, but the morbid process (hypertrophy and hyperplasia) was confined to certain specific regions. The histologic manifestations of hypertrophy and hyperplasia were accompanied by those of involution. This was to be expected because the clinical condition, hyperthyroidism, had been present in these cases for a number of years. Thus the diphasic cycle of the disease process had been completed many times in certain localized areas of those glands. It would, therefore, not be possible to have the histologic changes characteristic of the active phases of the disease, the hypertrophy and hyperplasia, without those accompanying the less active phase, namely, the involutional changes. The size of the nodules varied from small ones to those as large as a man's fist. The larger ones were found more frequently in older people in whom the duration of the disease had been longer and in these cases the capsules were more clearly defined, probably as the result of a greater degree of pressure atrophy exerted over a longer period of time. These cases, clinically and pathologically, seemed to represent a chronic manifestation of the same disease process which appears more acute in typical exophthalmic goiter. It has become firmly fixed in the minds of some observers that a nodule of considerable size with a capsule around it is necessarily a neoplasm and, therefore, an adenoma. That this idea is incorrect would seem to be proved by this study. Nodules of all sizes may develop as a result of involution of a previously diffuse hyperplasia of the thyroid or because localized specific regions of the gland become the site of the disease process while the intervening parenchyma retains the appearance of normal thyroid tissue. The size and encapsulation of the nodules or tumefactions in either group is in direct proportion to the length of the disease process and the age of the patient, or the direct ratio of the frequency of the completion of the disease cycles. This study, then, shows that in 52 per cent of our cases of nodular goiter with hyperthyroidism, the nodular elements did not represent true benign neoplasms or adenomas. Careful examination of these nodules revealed the fact that the pattern suggests the microscopic appearance of hypertrophy and hyperplasia rather than that of in recognizable neoplasms of the thyroid gland.

It would seem that the morbid processes may involve only the regions of the thyroid not only in the more active states but also in the localized areas of hypertrophy and hyperplasia but that the and inactive states as shown by the delimited area of the thyroid of hypertrophy, the parenchyma between the nodules is apparently being normal.

In 34 per cent of the cases in this study the thyroid gland was composed of involutional nodules. In 52 per cent of the cases the goiter had resulted from a regional involvement of the thyroid.

the same pathologic process, so that it would appear that the formation of a nodular goiter must be considered as one of the final stages or pathologic sequelae of the clinical entity, hyperthyroidism. In a relatively small percentage (only 8 per cent in our series) was the nodular element due to a true benign neoplasm.

The older patients with hyperthyroidism associated with a nodular goiter are those who have survived the disease long enough for the nodules to develop in the thyroid glands. The fact that they are better operative risks and are less apt to have severe postoperative reactions than the younger patients with a more acute clinical picture and a diffuse hypertrophy and hyperplasia of the thyroid gland, would tend to bear out this statement.

In the last few years, references to "toxic adenoma" and "hyperfunctioning adenomatous goiter" have frequently appeared in American medical literature. These terms are obviously incorrect and misleading. In the small percentage of cases in which true benign neoplasms are associated with hyperthyroidism the histologic manifestations of hyperactivity of the parenchyma have been demonstrated throughout the gland as a whole, so that the neoplasm should be regarded merely as a coincidental pathologic lesion.

There is no proof that the secretion of a benign tumor can affect the organism as a whole or that it can give rise to toxic manifestations.

At present it is impossible to make a differential clinical diagnosis between a true benign neoplasm, an involutinal nodule and a tumor resulting from a localized area of hypertrophy and hyperplasia with involution in a patient with hyperthyroidism. Nodular goiter with or without hyperthyroidism and diffuse goiter with or without hyperthyroidism would seem to be a more accurate and an equally efficacious clinical distinction.

## COMMENT

Modifications of the combined suprahyoid and lateral dissections of the neck may be allowed in tuberculosis and Hodgkin's disease. In such cases the sternocleidomastoid muscle may be preserved, the cervical nerves are spared, and the internal jugular vein is taken only as a matter of convenience. In metastatic carcinoma, in carcinoma of the branchial cleft and in endothelioma of the neck the procedure is never more limited than that outlined in the foregoing description of the combined operation. Sometimes additional structures must be removed, occasionally the hypoglossal nerve and the digastricus and stylohyoid muscles must be dissected out because of their involvement within a large carcinomatous mass. Even the vagus nerve sometimes must be sacrificed. Removal of less than the whole of the deep cervical chain in metastatic carcinoma involving these groups of glands is just as inadequate as a simple amputation without axillary dissection for carcinoma of the breast.

Simple suprahyoid dissection is an absolute safeguard in cancer of the lip. It should be employed early in the course of the disease before gross involvement of glands has taken place, and should not be delayed until there is little doubt regarding the malignant nature of the swelling or enlargement of the glands beneath the chin. Microscopic examination of the glands may fail to reveal metastatic carcinoma in a surprising number of instances, but statistical studies show that in a high percentage of the cases in which dissection of the neck is not employed the patients return to the physician later on account of metastases. This is especially true of the cases which show involvement of the muscle of the lip or in which there is a slight degree of differentiation of cells. Dissection of the neck in the suprahyoid region is not mutilating, no vital structures are in danger, and the procedure is simple and can be accomplished by one with a limited surgical experience, on the other hand, the results from the standpoint of protection are absolute.

The combined suprahyoid and lateral dissection for metastatic carcinoma in the deep cervical chains is almost as satisfactory even in the presence of gross involvement of these glands, and in the majority of instances gives a complete and permanent block to the spread of the disease by metastases. While it is true that cures are relatively few in carcinoma of the tongue or the pharynx, it is the inability to get rid of the primary focus and the infiltration of the floor of the mouth or pharynx and not the inability to control metastases that accounts for the failure. The later dissection, while not as simple as the suprahyoid, can be easily mastered, and is not a formidable procedure for surgeons who are skilled in handling tissues, even though they have had little experience in operations on the neck. Even in this extensive procedure, mutilation is negligible. The bilateral combined operation is seldom employed,

grams made of the leg and foot after injection of sodium iodide into the femoral artery indicated a good arterial supply to the leg. The medium stayed in the arteries for a considerable length of time, none of it being in the arteries after an hour, however, except probably a small amount which stuck to the wall. On February 12, the skin showed a mottling appearance up to the knee and this mottling was extending medially to the perineum. On February 17, the leg had increased markedly in size and had apparently lost all sensation. A definite line of demarcation was not present. The odor was typically

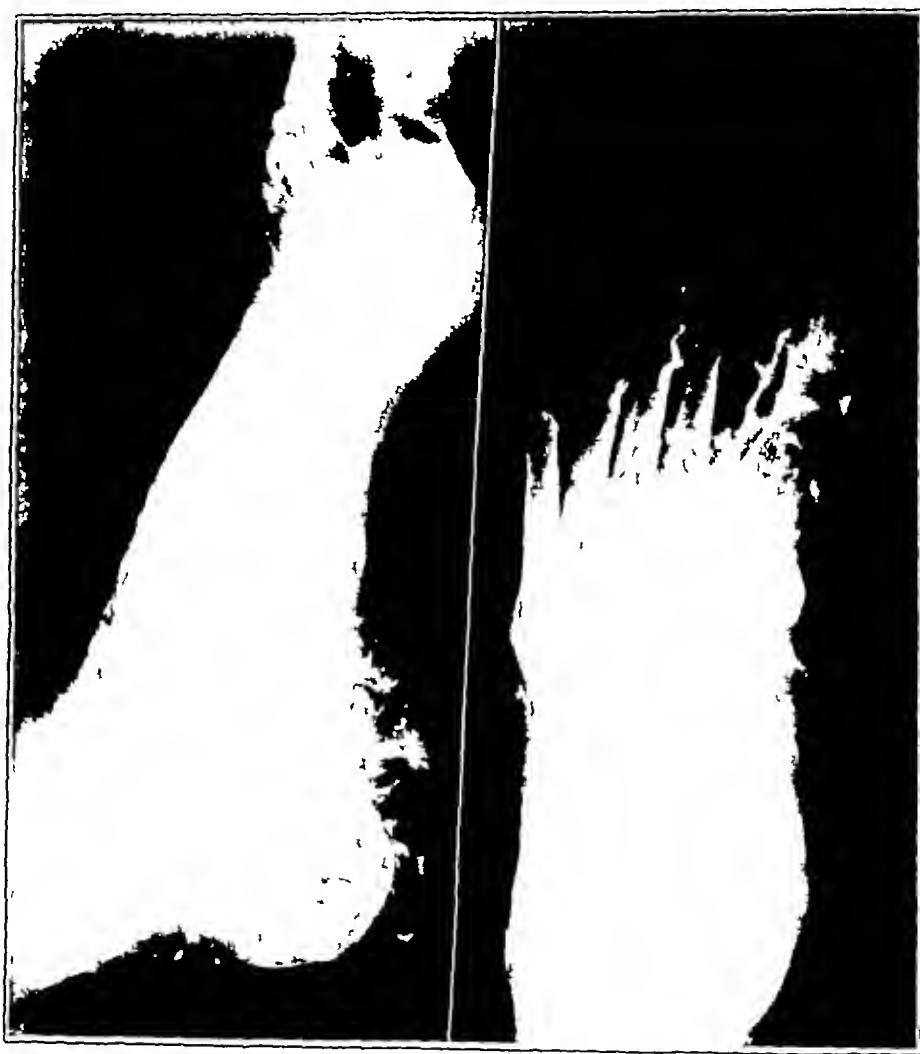


Fig 6 (case 6)—Arterial tree in the foot showing arterioles blocked by disease in a case of senile gangrene. The solution is seen being retained in the arterioles and capillaries.

gangrenous. On February 20, the lower half of the thigh in front and the thigh to the buttocks posteriorly showed moist gangrene. The patient was unconscious. The blood pressure was decreased, and catheterization was necessary. The patient recovered ability to void, but showed no particular improvement. He died on March 1.

In this case also the results were unfavorable, and it was again demonstrated that sodium iodide is dangerous if there is sufficient obstruction to cause its

but may be performed without fear of serious consequences. It is wise to allow sufficient time between the two operations for the establishment of collateral circulation.

Apropos of recent discussions concerning the anesthetic to be employed in complete dissection of the neck, it has been our experience that the most satisfactory anesthetic is light ether, that is, a minimum of ether and a maximum of air. Local anesthesia with procaine hydrochloride, nitrous oxide and oxygen, ether and chloroform have been employed. Ether is preferred because postoperative pneumonia and mortality have been negligible and because the patients have been more comfortable following this type of general anesthetic. With local anesthesia the discomfort of lying on the table throughout the long period required for a painstaking operation of this sort is a point to be weighed. There is more oozing under nitrous oxide because of the unavoidable cyanosis, be it ever so slight, in addition, the method of administration is more difficult because of the proximity of the operative field to the face. Obstetric chloroform would be the ideal anesthetic in the hands of an anesthetist absolutely familiar with the drug.

Ether should be administered intrapharyngeally with some machine adapted to furnish air under positive pressure. The intratracheal method of administering ether anesthesia is to be avoided because of the high mortality when this method is used because of the difficulty of administration, and because it is not an improvement on the intrapharyngeal method.

retention in the vessels for an unduly long time. In arteriosclerotic gangrene, as previously mentioned, the capillaries and arterioles are markedly narrowed, and unquestionably in this type of case, the injection is not to be used.

#### SUMMARY

1 Roentgenologic examination after intra-arterial injection of sodium iodide accurately reveals the condition of the blood vessels. Such injection is apparently harmless when there is good capillary circulation and a free return of blood into the general circulation. The method is apparently safe.

2 In aneurysms of the extremities, both arterial and arteriovenous, valuable information is gained in regard to the blood vessels entering and leaving the aneurysms and the collateral circulation, which may be of great assistance in determining the method of treatment.

3 In spontaneous gangrene resulting from venous or arterial obstruction, the method is not safe and probably should not be used. It is contraindicated in moist gangrene with venous obstruction, and also in arteriosclerosis because of the narrowing in the arterioles and capillaries. In thrombo-angitis obliterans, the capillaries are usually much more normal, and there is better collateral circulation, therefore, in this condition, the method should not be harmful.

# USE OF INTRA-ARTERIAL INJECTIONS OF SODIUM IODIDE IN DETERMINING CONDITION OF CIRCULATION IN THE EXTREMITIES

REPORT OF CASES \*

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Impairment of the circulation in the extremities due to diseased blood vessels, which results in gangrene and the symptoms accompanying it, is of ever growing importance. The conditions responsible for these failures of circulation may be considered as aneurysms of various types and obstructions to the arteries and veins. The acute obstructions may be due to emboli or thrombi obstructing important vessels, the result of which may be gangrene if either the arterial or venous blocking is sufficiently complete. The more chronic types of gangrene are the result of arterial disease, and clinically and pathologically, these are recognized as (1) the arteriosclerotic type which embraces senile and diabetic gangrene, (2) thrombo-angitis obliterans (Buerger's disease) and (3) arterial spasm (Raynaud's disease).

Each of these three types of disease of the blood vessels differs distinctly in its pathologic changes. In the arteriosclerotic type, the entire arterial system is involved, the capillaries and arterioles being seriously involved, and the development of a compensatory collateral circulation is hardly possible. In thrombo-angitis obliterans, the capillaries and arterioles are not affected to a corresponding extent, and the development or improvement in the collateral circulation is possible. In Raynaud's disease, an arterial spasm exists rather than permanent changes in the blood vessels. This knowledge should be kept in mind, and efforts at treatment of patients with gangrene or impending gangrene of the extremities should be guided accordingly.

In the arteriosclerotic type, in spite of many reports to the contrary, arterial sympathectomy is probably not indicated. If methods other than palliative measures or amputation are used, obstruction of the venous return of the blood from the extremity should at least theoretically be resorted to by partially blocking the femoral vein and thereby utilizing to the fullest extent the diminished amount of blood which passes through the small arteries. It may be that in some cases the good results which have followed arterial sympathectomy or the injecting of alcohol around the artery for the same purpose, as practiced by

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\* Read before the Southern Surgical Association, Augusta, Ga., December, 1927



# STUDIES IN INTESTINAL OBSTRUCTION

## III SIMPLE OBSTRUCTION A STUDY OF THE CAUSE OF DEATH IN MECHANICAL OBSTRUCTION OF THE UPPER

### PART OF THE INTESTINE \*

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AND

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MINNEAPOLIS

There are two fairly distinct types of intestinal obstruction, clinically as well as experimentally, in one the continuity of the intestinal canal has been interrupted, in the other gross evidence of damage to the obstructed segment exists in addition to a break in the continuity of the tract. These forms have aptly been described as simple and strangulation obstruction.<sup>1</sup>

Early clinicians and investigators thought that in simple occlusion of the bowel, the wall became permeable to bacteria in the intestine, and peritonitis and bacterial invasion of the organism brought about a lethal outcome.<sup>2</sup> Such a contention has been set aside by subsequent investigation, as well as by the frequent opening of the abdomen, under aseptic conditions of both patients and dogs with obstruction

Amussat<sup>3</sup> is generally looked on as being the originator of the intoxication theory for the explanation of symptoms and death in intestinal obstruction. This view, which today has most investigators and clinicians as its adherents, accounts for the lethal outcome in the formation and absorption of potent toxins above the point of obstruction. Braun and Borrutau,<sup>4</sup> unable to verify the presence of a toxic body in the obstructed intestine that is not present normally, ascribed death to splanchnic paresis and shock. Hartwell and Hoguet<sup>5</sup> inclined

\* From the Department of Surgery of the University of Minnesota

\* Presented before the Minnesota Pathological Society

1 Hausler and Foster. Studies on Acute Intestinal Obstruction, II. Acute

Strangulation, Arch Inter Med **34** 697 (Nov.) 1924

2 Khautz, A. Zur Frage der Bakteriämie bei Ileus und postoperativen

Darmlähmung, Arch f klin Chir **88** 412, 1909. Borzky, C, and Genersich, A

Beitrage zur lokal diagnose der inneren Darm Okklusionen und zur Frage der

Autointoxikation, V, Bruns Beitr z klin Chir **36** 448, 1902

3 Amussat. Relation de la maladie de boursousais, Paris, 1838, quoted by

Enderlen and Holz. Ueber die Resorption bei Ileus und Peritonitis, Mitt a d

Grenzegeb d Med u Chir **23** 755, 1911

4 Braun W, and Borrutau, H. Experimental kritische Untersuchungen

uber den Ileus Tod, Deutsche Ztschr f chir **96** 544, 1908

5 Hartwell, J A and Hoguet, J P. Experimental Intestinal Obstruction

in Dogs with Especial Reference to the Cause of Death and the Treatment by

Large Amounts of Normal Saline Solution, J A M A **59** 82 (July 13) 1912

Sampson Handley,<sup>1</sup> in senile gangrene, have been due to the partial obstruction of the femoral vein by the swelling of the surrounding tissue following the operative procedures.

In the second type of gangrene (Buerger's disease), there is a possibility of an improvement of the collateral circulation, and with the lower extremity involved, the ligation of the femoral artery as practiced by Dr. Dean Lewis<sup>2</sup> would possibly be the treatment of choice.

The uniformity of the arterial channels and their collateral circulation can usually be relied on to guide one to the most favorable site for amputation. But because one cannot tell the exact condition of the vessels, one may sacrifice an unnecessary length of leg, or again one may amputate at too low a level, so that the condition for which amputation was performed would not be relieved. In order to determine more definitely the location of the vascular obstruction, many methods have been suggested, no one of which has been entirely satisfactory. The Moskowitz method is well known, and the test depends on the alteration of the color of the skin which results from the alternate application and removal of a tourniquet. But this method is often inadequate and unreliable.

The change in the temperature of the foot or toe produced by the application and removal of a tourniquet, as recommended by Brooks<sup>3</sup> following some excellent observations, is more promising and with development may be of great value. The apparatus consists of a thermocouple mounted in a hypodermic needle and a galvanometer. It permits of accurate measurements of the temperature of the foot and records accurately rapid change in temperature. The tourniquet is applied for ten minutes, and the temperature of the tissues of the extremity falls to room temperature. It was found that with the removal of the tourniquet the temperature in the tissues of the normal extremity rapidly rose to normal. On the other hand, in the tissues of an extremity in which there was impairment of the arterial blood supply, the release of the tourniquet was not followed by a prompt rise in temperature.

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1 Handley, W. Sampson. Treatment of Gangrene of the Extremities, *Proc Roy Soc Med* 20: 485 (Feb) 1927.

2 Lewis, Dean. Spontaneous Gangrene of the Extremities, *Arch Surg* 15: 613 (Oct) 1927, Lesions of the Blood Vessels of the Extremities, *South M J* 20: 421 (June) 1927.

3 Brooks, Barney. Intra-Arterial Injection of Sodium Iodide, *J A M A* 82: 1016 (March) 1924, Diseases of the Blood Vascular System of the Extremities, *J Bone & Joint Surg* 6: 326 (April) 1924, New Method for Study of Diseases of the Circulation of the Extremities, 7: 316 (April) 1925. Brooks and Jostes. A Clinical Study of Diseases of the Circulation of the Extremities, *Arch Surg* 9: 485 (Nov) 1924.

to the belief that dehydration in itself is the most important factor Hausler and Foster<sup>6</sup> stated that death in cases of simple occlusion of the bowel can be accounted for on the basis of starvation alone

Since Hartwell and Hogue<sup>5</sup> first made known the efficacy of saline in prolonging the life of the animal in which an obstruction had been established experimentally, this observation has been corroborated by a large number of investigators and clinicians.<sup>7</sup> Extensive experimentation by Haden and Orr<sup>8</sup> relative to the protection that sodium chloride solution afforded the animal<sup>8</sup> with intestinal obstruction would indicate that the virtue of the saline lay in the drug per se. They were unable to obtain the same beneficial effect from other drugs containing either the sodium or the chloride radical alone. They believed that sodium chloride combines with the toxic bodies responsible for the fatal issue in intestinal obstruction, rendering them inert.

In a previous study,<sup>9</sup> by experiments on animals we were unable to ascertain the presence of toxic bodies in the intestine with simple obstruction not found in the normal intestine. The intestinal contents of dogs with an obstructed intestine to which salt solution had been administered were also toxic on injection. This would indicate that unusual toxins, if present, were not rendered innocuous within the bowel.

In another study<sup>10</sup> it was found that the intestine, with interruption of its continuity, was not abnormally permeable to histamine. In this investigation we have been concerned only with simple obstruction with particular reference to the evidence that abnormal absorption from the obstructed bowel is responsible for the death of such an animal.

### 6 Hausler and Foster Studies on Acute Intestinal Obstruction III

Simple Obstruction, Arch Inter Med **36** 31 (July) 1925  
 7 Dixon, C. The Value of Sodium Chloride in the Treatment of Duodenal Intoxication, J A M A **82** 1498 (May 10) 1924 Haden and Orr Chemical Changes in the Blood of Man After Acute Intestinal Obstruction, Surg Gynec & Obst **37** 465, 1923, Hausler and Foster (footnote 6) MacCallum, W. B., Lintz, H., Vermilye, H. N., Leggett, T. H., and Boas, E. The Effect of Pyloric Obstruction in Relation to Gastric Tetany, Bull Johns Hopkins Hosp **31** 1, 1920 McVicar, C. S. The Clinical and Laboratory Findings in Certain Cases of Obstruction on the Upper Gastro-Intestinal Tract The Role of Blood Chemistry in Diagnosis, Prognosis and Treatment of this Condition, Am J M Sc **169** 224, 1925

8 Haden, R. L., and Orr, T. G. Chemical Changes in the Blood of the Dog After Obstruction on the Duodenum, J Exper Med **37** 365 and 377, 1923, *ibid* **39** 321, 1924, *ibid* **38** 55, 1923  
 9 Wangenstein, O. H., and Chunn, S. S. Studies in Intestinal Obstruction A Comparison of the Toxicity of Normal and Obstructed Intestinal Content, Arch Surg, to be published  
 10 Wangenstein, O. H., and Loucks, M. Studies in Intestinal Obstruction, II The Absorption of Histamine from the Obstructed Bowel, Arch Surg, to be published

Still another method of determining the condition of the circulation in the extremities is by the injection of sodium iodide into the arteries and by roentgenologic examination. Brooks is also credited with making and publishing important experimental and clinical observations in the use of this method. He recommends the exposure of the femoral vein and artery in Scarpa's triangle, and with the vein and artery clamped above, 10 cc of 100 per cent sodium iodide is injected into the artery with a syringe and needle and a roentgen-ray exposure is rapidly made on a sensitive plate. The pain is severe, and a short gas anesthesia is required. I have made use of this method in six patients since the publication of Brooks' work. The technic employed has been slightly different in that a light spinal anesthesia was used in four patients, this seemed to have the advantage of securing the cooperation of the patient. It was also not found necessary to expose the vessels by an incision, but the solution was easily injected with a needle through the skin, while an assistant exerted pressure over the artery and vein just below the inguinal ligament. The results of my experiences cause me to both recommend and to condemn the method. It is because of the unfavorable results, as much as the favorable, that I am prompted to make a record of my observations.

Three of the six cases that are reported, occurred in patients with aneurysms—one of the popliteal artery, one an arteriovenous aneurysm of the femorals and one an aneurysm of the first part of the brachial artery. The results in these three cases were satisfactory, and the information gained was invaluable. The other three cases occurred in patients with gangrene of the toes or feet. Two were of the senile or arteriosclerotic type, and the other was a moist gangrene due to venous thrombosis of the femoral vein associated with sepsis. In these cases, the results were decidedly unfavorable. While the arterial tree showed perfectly and the condition of the circulation was revealed thoroughly, the damage to the already diseased and narrowed arterioles and capillaries from the sodium iodide was evident, in two instances, the gangrene spread rapidly, necessitating a high amputation in one, while death followed in the other.

#### REPORT OF CASES

CASE 1—E S, a colored man, aged 30, entered the hospital on Nov 8, 1922, because of chronic ulcers of the leg which would not heal. Physical examination at this time revealed the classic signs of an aneurysmal ligament.

The diagnosis was chronic syphilitic ulcers of the left leg and arteriovenous aneurysm of the left femoral artery and vein. Healing of the ulcers occurred following the application of dressings and antisiphilic treatment. The patient left the hospital on December 11, with the ulcers improved, but the condition of the aneurysm was the same. The patient reentered the hospital on Jan 16, 1923, with ulcers of the left ankle and poor circulation in the left leg. Results of physical examination at this time were essentially the same as those on the

As considerable experimentation has been done in this field, a number of the experiments reported in this study have been performed by other investigators. In order to be able to interpret the results of such experi-

*Data on Dogs in Experimental Intestinal Obstruction*

Dog	Nature of Procedure	Operation	Day After	Blood			Urine and Vomitus	
				Mg per 100 Cc.	Chlorides	Amount	Nonprotein	Protein
82	Duodenal obstruction of the severed		0	11.80	640	125	0.90	0.00
Weight, 40 pounds (18.1 Kg)	Intestine, 12/22/26		1	26.60	450	1,250	8.67	0.00
			2	10.20	430	316	4.41	0.00
			3	40.13	430	650	5.66	0.00
			4	38.73	360	160	2.66	0.00
			5	41.62	340	600	5.32	0.00
			6	69.20	310	620	5.04	0.00
			7	83.16	320	640	4.10	0.00
Died 12/29/27, weight at death, 32 pounds (14.5 Kg)								
83	Duodenal obstruction of the severed		0	10.26	490	90	1.10	0.00
Weight, 29 pounds (13.2 Kg)	Intestine, 12/22/26, given 400 cc 2% saline subcutaneously once daily		1	19.13	460	865	4.66	0.00
			2	21.46	460	1,500	6.44	0.00
			3	18.66	660	1,010	7.08	0.00
			4	16.86	740	2,200	6.67	0.00
			5	16.80	660	2,225	7.62	0.00
			6	20.53	620	2,700	5.23	0.00
			7	16.66	600	870	6.03	0.00
			8	27.30	480	1,850	6.68	0.00
			9	18.26	410	1,025	4.37	0.00
			10	17.87	390	1,300	3.95	0.00
			11	14	470	1,625	6.40	0.00
			12	16.30	620	740	3.33	0.00
			13	14.47	410	110	1.54	0.00
			14	16.64	400	160	3.20	0.00
			15	16.38	265	265	2.30	0.00
			16	18.20	120	60	2.40	0.00
			17	16.40	310	100	2.40	0.00
Dog died 1/10/27								
84	Duodenal obstruction of the severed		0	14	530	2,500	4.42	0.00
Weight, 39 pounds (17.7 Kg)	Intestine and gastrosplenostomy, 1/6/27 no saline given		1	14.47	400	2,000	3.38	0.00
			2	28.36	350	2,000	3.38	0.00
			3	26.20	250	2,000	5.27	0.00
			4	18.20	310	440	1.52	0.00
			5	66.93	260	1,000	0.30	0.00
			6	84.46	260	450	4.95	0.00
			7	119.06	250	870	7.40	0.00
Died, weight, 29 pounds			8			1,750	6.70	0.00
85	Duodenal obstruction and gastro		0	9	600	125	1.20	0.00
Weight, 40 pounds	enterostomy, 2/7/27, saline given		1	14	440	460	6.37	0.00
	subcutaneously, 400 cc 2% saline once		2	16.08	430	2,700	6.60	0.00
	daily		3	15.78	360	8,200	8.76	0.00
			4	14.32	610	1,075	3.70	0.00
			5	17.75	250	1,400	4.66	0.00
			6	9	480	630	3.40	0.00
			7	18.60	410	600	3.87	0.00
			8	16.60	440	50	1.25	0.00
			9	16.86	370	600	2.43	0.00
			10	17.40	430	600	2.60	0.00
			11	23.20	460	300	1.66	0.00
			12	14	420	250	1.76	0.00
1/7/27, dog in satisfactory condition, weight 34 pounds (15.4 Kg), vomits occasionally								

\* In these experiments the urine and vomitus were collected together. The dogs were allowed to drink water.

ments with any judgment, we felt that it was necessary to make our own observations. Since the results of a number of the experiments to be cited are fairly well known and established, the experimental procedures will not be listed in detail.

first admission. Roentgen-ray examination of the arterial tree showed the connection of the varix to be a wide communication between the artery and vein. Operation confirmed the diagnosis of an aneurysmal varix, and the afferent and efferent arteries were ligated and divided. The patient recovered from the operation and the ulcers about the ankles healed rapidly. When the patient was dismissed from the hospital on March 16 the circulation in the leg and foot was fairly good. A low localized bruit could still be heard over the middle third of the thigh. The patient reentered the hospital on June 30 because of fracture of the base of the skull. He recovered completely from this condition. On July 11, the femoral artery was again injected with 10 cc of 100 per cent sodium iodide, and a roentgenogram was made which showed the ligated ends of the artery, the profunda femoris and a large number of small collaterals connecting the two portions of the artery. The patient was discharged from the hospital on July 25, is improved.

The information gained by the arterial injection previous to the operation was of value in that it showed the inadvisability of attempting to separate the artery and vein and suture the separate openings, which method probably would otherwise have been attempted.

CASE 2—D. P., a colored man, aged 46, was admitted to the hospital on July 19, 1924, his chief trouble being granuloma inguinale which had produced a urethral fistula. He had also complained of pain in the left leg which caused him to limp or to have difficulty in walking because of a "knot" at the posterior part of the joint of the knee. A diagnosis of popliteal aneurysm was made. Twenty cubic centimeters of 100 per cent sodium iodide was injected into the femoral artery, and a roentgenogram was made. This showed an enormously dilated femoral artery of the left leg with a popliteal aneurysm with partly calcified walls. The condition of the entire femoral artery as shown by injection of iodine indicated that operative treatment was not advisable.

Without the roentgen-ray observations I think unquestionably that an intra-arterial suture of the aneurysm would have been attempted, this I am sure would have resulted in failure, and most likely in gangrene of the leg.

CASE 3—A. A., a colored man, aged 39 entered the hospital on Aug 17, 1927, suffering from gunshot wounds of the chest and arm. One of the bullets had penetrated the right axillary region and had produced a huge hematoma in the right axilla. There was also considerable swelling in the region of the right shoulder. The immediate swelling subsided and about one month after admission a small swelling was noticed in the right axilla just at the junction of the axillary and brachial arteries. This swelling gradually increased in size and became pulsating. About six weeks after admission, the swelling was about the size of a lemon and showed all the classic signs of an aneurysm. Eight cubic centimeters of 100 per cent sodium iodide was injected directly into the aneurysm and a roentgenogram was made which showed that the aneurysmal sac and the arteries below it were well injected. Immediately after the injection the extremity showed some paleness which rapidly disappeared without detrimental effects. One week later the patient was operated on and a metal clip was applied around the third part of the axillary artery and tightened until the radial pulse was practically obliterated. At the present time the aneurysm has almost disappeared and the circulation of the extremity shows signs of slight venous obstruction.

The profunda artery was here revealed, leaving the brachial immediately adjacent to the sac of the aneurysm. It was found so intimately associated with the sac that the contemplated anastomotic suturing was abandoned.

# METHOD

All experiments were performed on dogs under ether anesthesia and aseptic technic. Severed gut obstructions were established largely in the duodenum, a few were established in the lower ileum and one in the lower part of the descending colon. At the point selected for obstruction, the gut was severed between "crushing clamps" and the ends of the bowel inverted "much as the stump of the appendix is treated in appendectomy.

The effect of giving salt solution was noted in some of the dogs with duodenal obstruction. In several animals gastro-enterostomy was established in addition to the high duodenal obstruction. Some of these animals were given salt solution, others were not. Division of the stomach beneath the diaphragm was practiced in a few animals with and without the subcutaneous administration of salt solution. In two animals the esophagus was ligatured in the neck. Duodenal fistulas were established in a number of animals. Salt solution was given to some of them.

When sodium chloride was administered, it was given subcutaneously, with a 50 cc syringe. In most instances, from 250 to 400 cc of a 2 per cent solution was given once a day. A 1 per cent solution was given to a few animals, 400 cc being given twice a day. The blood urea and chlorides were determined daily on all animals. Blood was obtained from the jugular vein or the vein on the outer aspect of the hind leg of the dog. Some of the animals were placed in metabolism cages and the nitrogen output in the urine determined. The nonprotein nitrogen in the urine was determined by the micro-Kjeldahl method of Folin and Denis<sup>13</sup> and the urea nitrogen of the blood by the method of Van Slyke and Cullen<sup>14</sup>. The blood chlorides were determined according to the method described by Gettler.<sup>15</sup>

Two of three dogs in which severed gut obstructions were established in the duodenum about 15 cm beyond the pylorus died within seventy-two hours. The increase of the nonprotein nitrogen in the blood and decrease of the chlorides observed by previous investigators<sup>16</sup> were

- 11 In some earlier experiments, it had been observed that animals occasionally survived ligature obstructions. In the animals that died or were killed, the obstruction was usually found incomplete at necropsy.
- 12 The distal end of the bowel, when the division was made in the small intestine, was anchored to the abdominal wall because it was noted that in some of the early animals in which this procedure was not practiced, intussusception of the distal loop not infrequently occurred.
- 13 Folin, O., and Denis, W. Nitrogen Determination by Direct Nesslerization, I. Total Nitrogen in Urine, J Biol Chem 25 473, 1916
- 14 Van Slyke, D D., and Cullen, G E. A Permanent Preparation of Urease and Its Use for Rapid and Accurate Determination of Urea, J A M A 62 1558 (May 16) 1914
- 15 Gettler, A O. A Method for the Determination of Death by Drowning, J A M A 77 1650 (Nov 19) 1921
- 16 Cooke, J V. Rodenbaugh, F H., and Whipple, G H. Intestinal Obstruction, A Study of Non-Coagulable Nitrogen of the Blood, J Exper Med 23 717, 1916
- Connors, J F., Killian, J A., and Eisberg, H B. Chemical Changes in the Blood in Intestinal Obstruction, Proc Soc Exper Biol & Med 20 357, 1923.
- Haden and Orr (footnote 8, first reference). Tillotson, W., and Comfort, C W. The Total Nonprotein Nitrogen and the Urea of the Blood in Health and in Disease as Estimated by Folin's Methods Arch Inter Med 14 620 (Nov) 1914.

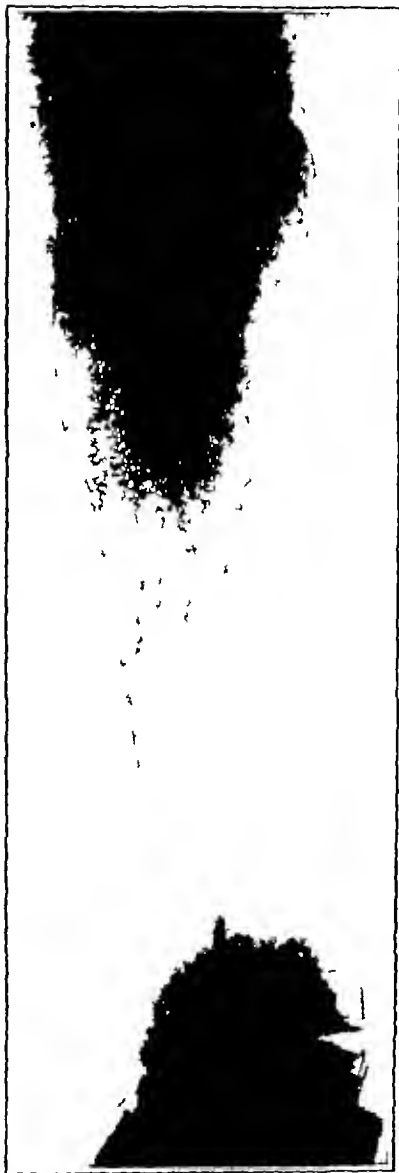


Figure 1



Figure 2

Fig 1 (case 1) —Arterial tree after ligation of the artery above and below the aneurysm. The roentgenogram of intra-arterial injection of arteriovenous aneurysm made before operation was lost.

Fig 2 (case 2) —Intra-arterial injection of popliteal aneurysm showing enormously dilated femoral artery above with aneurysmal sac in popliteal space.



noted The third dog survived the procedure seven days.<sup>17</sup> Two dogs with obstruction in the lower part of the ileum survived four days. In a group of ten dogs given from 250 to 400 cc of a 2 per cent salt solution subcutaneously, the average length of life following duodenal severed gut obstruction was seven days. Two animals with this type of obstruction, were given saline solution for one week, one animal survived eighteen days, the other, nineteen.

Severed obstructions of the same nature were made in two dogs, and a posterior gastro-enterostomy was added beyond the duodenojunal flexure. One of these animals survived two days, the other, nine. The changes in the blood chemistry present in animals with simple duodenal occlusion were observed. In two other animals, severed duodenal obstructions were established, gastro-enterostomy was performed and a linear division of the pyloric sphincter muscle (Rammstedt procedure) without incising the mucosa was practiced. The outcome was the same as in the animals in which the pyloric sphincter was intact, both died within seventy-two hours. Three dogs with a severed duodenal obstruction and an added gastro-enterostomy, were given saline subcutaneously for a week. One died two weeks after the original procedure from an obstruction due to an adhesive band lower in the intestinal tract. Another died from an extensive slough over the hind quarters where the hypertonic saline had been injected twelve days after the obstruction was established. The other dog was alive and well almost six months later. This dog became somewhat emaciated during his convalescence and vomited considerably. Occasional vomiting was noted at the last observation. Material alteration in the blood metabolites was not observed in any of the latter animals to which salt solution was given temporarily. An increased excretion of nitrogen, however, was observed in the urine. Complete duodenal fistulas were established in three animals at the same level at which obstruction had been established in the other dog. The proximal segment was drawn out through a small stab wound and sutured to the abdominal wall, leaving the lumen patent. The distal end was inverted and anchored to the parietal peritoneum. These dogs died three days later. The changes in the blood chemistry noted by Walters, Kilgore and Bollman,<sup>18</sup> were observed in these animals. Two of three other animals in which the same operative procedure was performed but which were given saline solution survived eight days, the other lived five days.

By making a T incision in the left rectus muscle in one dog, easy access was had to the cardiac end of the stomach. This was divided as

<sup>17</sup> Throughout this work on intestinal obstruction, it has been noted that larger dogs stand obstruction better than small animals.  
<sup>18</sup> Walters, W., Kilgore, A. M., and Bollman, J. L. Changes in the Blood Resulting from Duodenal Fistula, J. A. M. A. 86 186 (Jan 16) 1926

because of fear of destroying the profunda. If the profunda had been obstructed, the entire collateral circulation, which was between the profunda and the circumflex vessels, would have been cut off, this would have resulted in gangrene of the arm.

CASE 4—Mrs J. C., white, aged 28, who entered the hospital on April 10, 1925, gave a history of having been delivered of a postmature, full term, dead fetus four weeks previously. Following this she had chills, fever and exquisite pain on the slightest pressure over the middle of Poupart's ligament. All the symptoms were aggravated, the leg became markedly swollen, and the foot began to turn black. A diagnosis of moist gangrene from thrombosis of the left femoral and iliac vessels was made. About six weeks later, a line of demarcation had been established at the ankle joint. At this time, 15 cc. of 100 per cent sodium iodide was injected into the femoral artery, and a roentgenogram was made which showed that the arteries of the leg were normal. There was

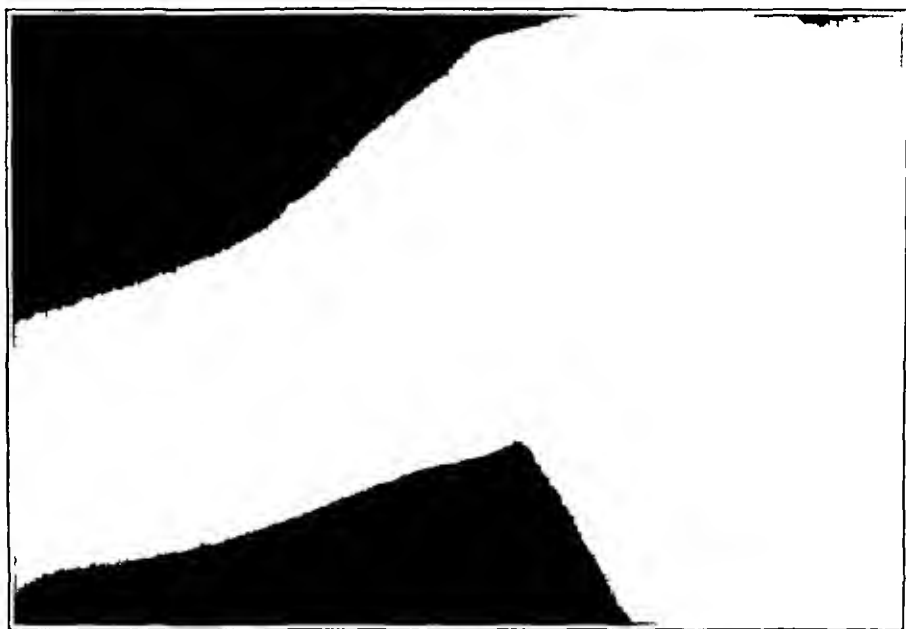


Fig. 3 (case 3)—Intra-arterial injection showing aneurysm of first part of brachial artery revealing profunda branch coming off close to the aneurysmal sac.

some blanching of the healthy tissue, and the gangrene which had become stationary immediately spread up the leg several inches. Two months later the leg was amputated at the seat of election. Primary union occurred, and the patient was discharged from the hospital on September 15 in a good condition.

The deleterious effect was evidently due to the irritation of the vessels by the solution, because the venous obstruction caused the drug to be retained overly long before it was returned to the general circulation.

CASE 5—A. P., a colored woman, aged 60, entered the hospital on Feb. 24, 1925, with a condition diagnosed as senile gangrene of the right foot, which extended up to the midtarsal joint. It was the usual dry type. After six weeks of expectant treatment, sodium iodide was injected into the femoral artery. Following the injection the leg became cold, and the circulation below the knee was seriously affected. Two days later, the patient died.

The dog high as possible and both proximal and distal ends inverted. The dog lived one day. In another animal the same procedure was repeated, but 400 cc of water was poured into the peritoneal cavity. The outcome was the same. In four other animals 400 cc of a 2 per cent sodium chloride solution was given once a day following the same procedure. One of these animals survived for a day, another, two days, a third dog lived seven days, and the other twelve days. Two dogs with ligation of the cervical esophagus died within two days.

In one animal, the descending colon was divided as low down as possible and the ends turned in. This dog survived the procedure for forty-two days. The increased nonprotein nitrogen found in the blood of animals with severed duodenal obstruction was not observed in this animal. The nitrogen excretion in the urine, however, was increased. At death the animal was markedly emaciated. The entire intestine was enormously distended, and the lower portion of the obstructed colon was packed tight with fecal material.

Two dogs were starved and dehydrated by being deprived of water for three days. Severed gut duodenal obstructions were then established. One of these animals survived for eight days. The changes in the blood chemistry found in dogs with simple duodenal obstruction were also observed in these animals. Two dogs with ileal obstructions were similarly starved and dehydrated without materially prolonging their lives.

Two dogs were dehydrated by being deprived of water and were given subcutaneous injections of pilocarpine and apomorphine to induce vomiting and added dehydration. Low values for blood chlorides were obtained in these animals without elevation of the blood urea nitrogen. The nitrogen output of the animals kept in metabolism cages was consistently high following duodenal obstructions. The urinary excretion of nitrogen was also increased in the animals that were given salt solution subcutaneously, and in which no material increase of the blood nonprotein nitrogen was observed.

# COMMENT

Clinicians and investigators alike concede the more serious import of obstructions high in the intestinal tract. In these experiments it has been recounted that dogs with duodenal obstruction usually die in seventy-two hours, whereas a dog with a severed gut obstruction low in the colon survived the obstruction for forty-two days. Starvation could well be assigned as the cause of death of the latter animal, in the case of the former, it is generally held that the formation and absorption of a potent toxin is responsible.

When, however, saline is administered to the animal with duodenal obstruction, his life may be prolonged for three weeks, as many investi-

The patient was old, and her general condition unfavorable, however, her death was apparently hastened by the injection

CASE 6—B F S, a white man, aged 86, entered the hospital on Feb 4, 1926, with a history of having been hurt in an automobile accident. Physical examination at this time showed a fairly well nourished man with abrasions on the right side of the chest and tenderness there, but roentgen-ray examination did not show fracture. While in the hospital the patient complained of a

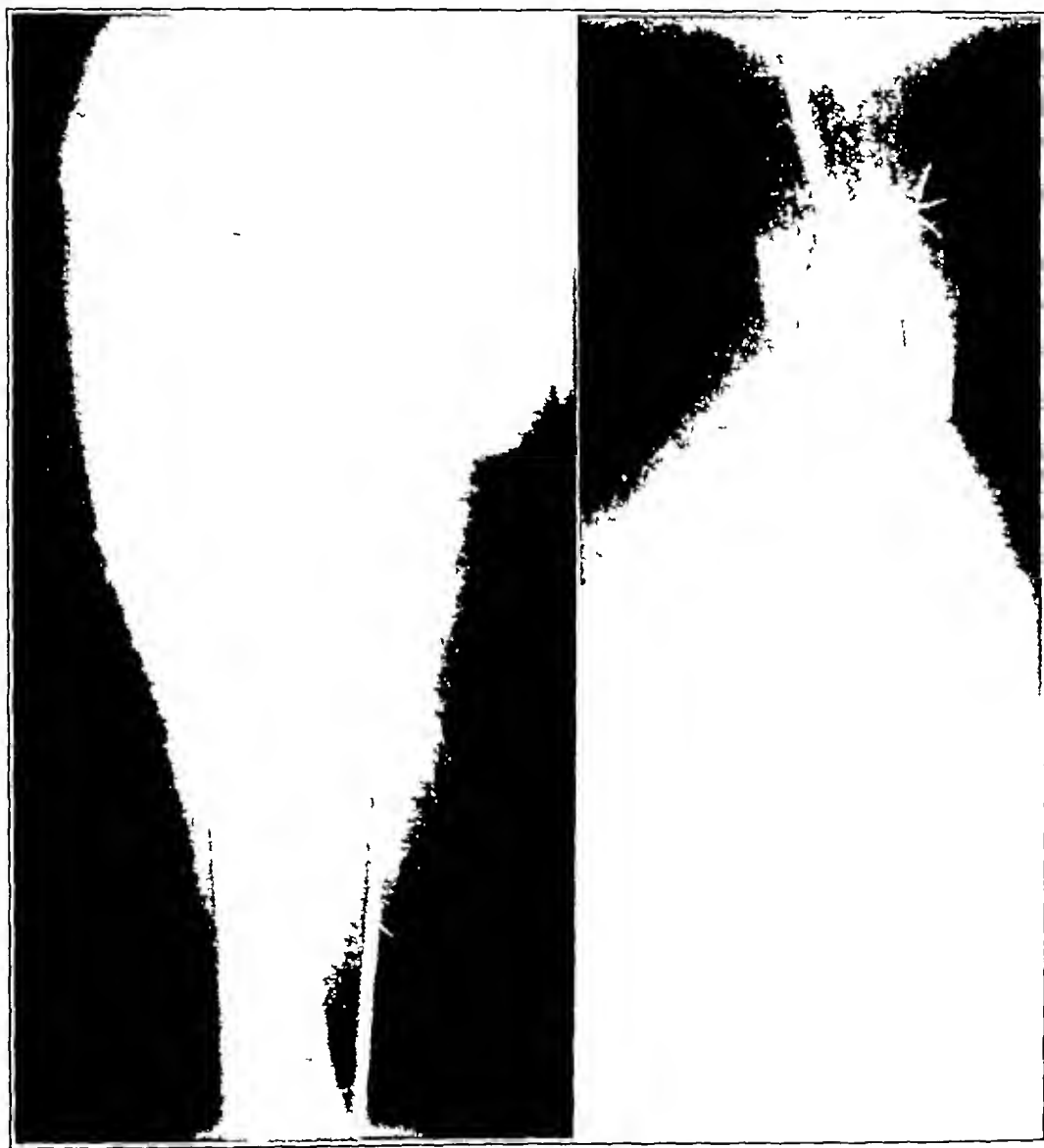


Fig 4 (case 4)—Arterial tree showing case of moist gangrene spreading higher following arterial injection

feeling of numbness in both feet and inability to move them as he had formerly done. The right foot showed a small gangrenous mass on the first and second toes. The great toe was involved to the size of about a five cent piece. Anesthesia involved all the toes of the foot. Both feet were numb, and the patient was unable to flex the metatarsal and phalangeal joints. There was



some pain involving the affected area. Touch and pressure sense was lost over the discolored portions, but pain, especially on the application of heat, was present. This numbness of the toes had become progressively worse during the last several years. The numbness during the last few days began to involve the right hand and fingers, particularly the fifth finger. The predominant loss was that of the sense of touch. The condition in the left leg became

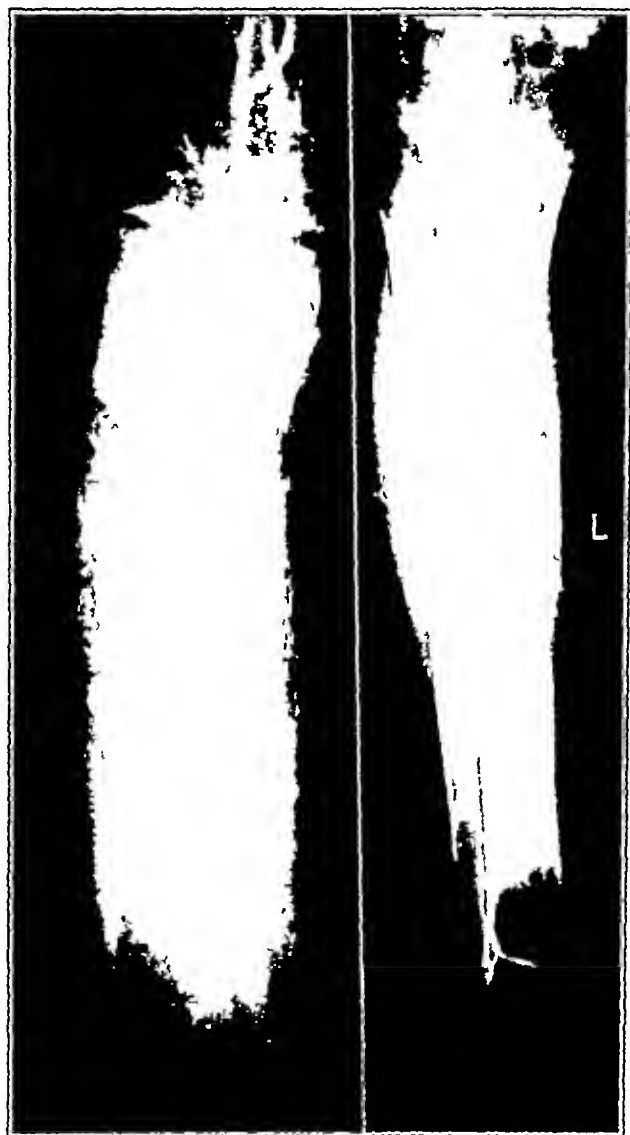


Fig 5 (case 5) —Arterial tree in case of senile gangrene. One view shows the leg upside down. While the main arterioles are open in both anterior and posterior tibias, senile gangrene occurred in the foot due to the obstruction of the arterioles and capillaries.

progressively worse while the patient was in the hospital. It became cold, motion was lost, and the leg was painful. On February 8, 15 cc of 100 per cent sodium iodine was injected into the left femoral artery, and roentgeno-

does not affect the outcome. When, however, sodium chloride solution is given to such an animal for a short period, changes in the blood do not occur, and he is able to live for a long time. Such an animal continues in good health except for the emaciation incident to the vomiting occasioned by the obstructed segment.

The virtue of sodium chloride in the treatment of the animal with a fistula or obstruction high in the intestinal tract probably represents, therefore, replacement therapy. A protective mechanism exercised through a detoxifying agency is unlikely. McCallum and his co-workers<sup>30</sup> and Gamble and Ross<sup>31</sup> are also of this opinion. It has been demonstrated by Haden and Orr<sup>32</sup> that other combinations of the sodium or chloride radical will not ward off early death in animals with duodenal obstruction. Hypertonic dextrose solutions similarly fail to do so. Walters and Bollman<sup>19</sup> have made the same observation in dogs with duodenal and gastric fistulas. Just why sodium chloride apparently alone should be able to fulfil this function is difficult to surmise, but the suggestion of Gamble and Ross<sup>31</sup> that it is particularly suited to replace the lost fluid and fixed base is probably correct.

Whipple and his co-workers<sup>33</sup> have shown that an increased destruction of protein occurs in intestinal obstruction. Haden and Orr<sup>32</sup> have made the same observation. Though injury to the kidney obtains in simple occlusion of the bowel, it is not likely that the increase in non-protein nitrogen of the blood is due to renal insufficiency, as has been suggested.<sup>34</sup> The fact that nitrogen is excreted in excess and that phenolsulphonphthalein is normally excreted<sup>35</sup> shows that renal failure is not present.

The increased excretion of nitrogen probably partakes of an acceleration of general body breakdown of protein. At any rate, the necrosis of the ends of the inverted bowel is not in itself responsible for the increased destruction.

An experiment often cited to indicate that death in obstruction is due to the absorption of potent toxins from the intestine is that per-

- 30 MacCallum, W. B., Lintz, H., Vermilye, H. M., Leggett, T. H., and Boas, E. (footnote 7, third reference)
- 31 Gamble, J. L., and Ross, S. G. The Factors in the Dehydration Following Pyloric Obstruction, J Clin Investigation 1 403, 1925
- 32 Haden and Orr (footnote 8, first and second reference)
- 33 Whipple, G. H., Cooke, J. V., and Stearns, T. Proteose Intoxications and Injury of Body Protein, J Exper Med 25 479, 1912
- 34 Brown, G. E., Eusterman, G. B., Hartman, H. R., and Kowntree, L. G. Toxic Nephritis in Pylorus and Duodenal Obstruction, Renal Insufficiency Complicating Gastric Tetany, Arch Inter Med 32 425 (Sept) 1923
- 35 Connors, J. F., Killian, J. A., and Eisberg, M. B. (footnote 16, second reference) Louria, H. W. The Blood Urea Nitrogen in Acute Intestinal Obstruction, Arch Inter Med 27 620 (May) 1921

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pital as showing hypertrophy of the exophthalmic goiter type, and in the remaining five patients (who had taken iodine before operation) were found the "typical exophthalmic goiter hypertrophy and hyperplasia of an iodine remission" (Rienhoff). Three of the five patients who took compound solution of iodine while in the hospital showed an average remission from iodine, with a drop in the basal metabolic rate from 37 to 15 per cent above normal, from 55 to 13 per cent above normal and from 57 to 31 per cent above normal, respectively. Three other patients had taken iodine just before entering the hospital. In the other five cases, iodine was not given. In only one of the thirteen patients was there evidence of heart disease (mitral stenosis and auricular fibrillation). Two other patients had edema, in one probably as a result of slight myocardial insufficiency and in the other of marked secondary anemia (hemoglobin content 58 per cent).

Of the other two patients in this group who did not show a striking degree of hypertrophy and hyperplasia, sections from the gland of one showed a small localized amount of hypertrophy and hyperplasia in a cystic area which contained an abundance of colloid. He was extremely obese, his postoperative basal metabolic rate was 26 per cent above normal and he had had a cystic nodule for five years. He presented doubtful clinical evidence of hyperthyroidism. In sections from the gland of the other patient it was possible to demonstrate three types of cellular structure—(a) typical "fetal" adenoma, (b) involution of the gland without hypertrophy and hyperplasia and (c) localized areas of hypertrophy and hyperplasia. When at rest, his pulse rate was 60 beats to the minute, and his basal metabolic rate fell from 28 per cent above normal to '16 per cent above normal after two days' rest in bed without medication. He complained only of tremor and loss of weight. Of this younger group, the eleven patients who were frankly thyrotoxic showed marked evidence of hypertrophy and hyperplasia of the exophthalmic goiter type which satisfactorily explains their clinical picture.

Except in two patients whose hemoglobin content (Sahli) was 58 and 60 per cent (the latter being the patient previously mentioned as having mitral stenosis and auricular fibrillation) anemia was not present. Including these two patients, the average hemoglobin content was 74 per cent, the average duration of the goiter (after its discovery) was four and a half years, and the average blood pressure was systolic 123 and diastolic 68. Three patients showed fairly high basal metabolic rates, 67, 65 and 55 per cent above normal, respectively, the average elevation above normal was 35 per cent. Although exophthalmos was not noted in any one of these cases, four patients showed a slight lagging of the lid (von Graefe's sign).

formed by Sauerbruch and Hyde<sup>36</sup> They denuded the abdominal wall of two rabbits and sutured the skin of one to that of the other Later, when a good crossed circulation had been established, an obstruction was created in one, following which the same toxic symptoms and death also occurred in the animal in which obstruction had not been established The outcome undoubtedly would have been the same if a duodenal fistula had been established in one of the animals

Sugito<sup>37</sup> claims to have isolated a toxin in the blood returning to the liver from the intestine in the mesenteric veins in dogs with intestinal obstruction When the serum from blood thus obtained was injected into the peritoneal cavity of rats, toxic symptoms were observed that were not elicited following the injection of blood from animals without obstructions Wilkie<sup>38</sup> and McLean and Andries,<sup>39</sup> however, have transfused large amounts of blood from dogs with intestinal obstruction to normal animals, without any untoward effect Wilkie also removed the intestinal contents from a dog with obstruction and placed them in the obstructed intestine of another dog without hurrying the development of toxic symptoms<sup>40</sup> A number of investigators<sup>41</sup> have demonstrated that intestinal contents obtained from animals with intestinal obstruction do not elicit toxic symptoms when placed in the bowel of a normal animal

Schonbauer<sup>42</sup> and Chenut<sup>43</sup> contended that abnormal absorption in simple obstruction may occur via the peritoneal cavity Schonbauer stated in support of his contention that iodine placed in the bowel of a dog with intestinal obstruction can be recovered from the peritoneal cavity He believed that death during obstruction is due to toxins permeating the wall of the bowel and being absorbed from the peritoneal cavity rather than to abnormal absorption from the lumen of the intestine Schonbauer and Löffler stated<sup>44</sup> that the antitryptic titer of the blood of

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36 Sauerbruch, F, and Hyde, M Weitere Mitteilungen ueber die paralyse bei Warmbeutern mit versuchen ueber Ileus and Uramie, *Ztschr f Exper path u Therap* 6 33, 1906

37 Sugito, S Ueber die Todesursache bei Ileus (Intoxicationstheorie), *Mitt a d med Fak d k Univ Kyushu u Fukuoka* 9 229, 1924

38 Wilkie, D P D Acute Intestinal Obstruction, *Lancet* 1 1135, 1922

39 McLean, A, and Andries, R C Ileus Considered Experimentally, *J A M A* 59 1614 (Nov 2) 1912

40 Wilkie, D P D Experimental Observations on the Cause of Death in Acute Intestinal Obstruction, *Brit M J* 2 1064, 1913 (footnote 38)

41 Chenut, A L'Eperimentation dans l'occlusion mechanique du jejunoleon, *Rev d chir* 45 474, 1926 (footnote 38)

42 Schönbauer, L Die Fermente in Ihrer Beziehung zu gewissen der Gallenblase und zum Ileus, *Arch f klin Chir* 130 427, 1924

43 Chenut (footnote 41, first reference)

44 Schönbauer, L, and Eöfler, E Ueber Ileus-serum, Experimentelle und Klinische Untersuchungen, *Wein klin Wchnschr* 38 135, 1925

has been assumed by many to account for the facts already mentioned.<sup>12</sup> Dilution alone must be an ineffective neutralizing mechanism, since these fluids are themselves either neutral or barely alkaline.<sup>4</sup> For example, to reduce the acidity of gastric juice from 1.40 to 3.5, it would be necessary to add three times its volume of a neutral fluid, whereas only three fourths its volume of pancreatic juice would be required, since it can completely neutralize more than its own volume of tenth normal hydrochloric acid. That the pancreatic juice is actually responsible for this regulation is made to appear more likely by the results of the experiments recorded in this article. All the foregoing factors have remained intact in them. By mere elimination of the external pancreatic secretion, therefore, neutralization in the stomach could not occur, and the contents of the stomach were constantly more acid than normal.

One finds frequent references in the literature to the rôle of bile in the neutralization of gastric acidity, the erroneous assumption being that bile is alkaline in reaction. All investigations have shown that hepatic bile is neutral. According to Drury, McMaster and Rous,<sup>13</sup> the influence of the gallbladder is such as actually to make the bile acid before it arrives at the intestine ( $pH$  from 5.1 to 6.8). It must be unlikely, therefore, that bile plays any part in the neutralization of gastric acidity.

Duodenal antiperistalsis, of course, must take place before pancreatic juice can enter the stomach. Roentgenologists have apparently rarely observed it,<sup>14</sup> though such evidence is merely negative. Recently, Bolton and Salmon<sup>15</sup> examined 100 persons, including many normal persons, with this point particularly in mind. They describe four different types of peristaltic movements in the duodenum. One of them consists of a contraction in the proximal duodenum which propels the opaque medium toward the pylorus, which, by its relaxation, permits the passage of the medium into the stomach. Such a relaxation with visible reflux was actually seen but six times, though the duodenal antiperistalsis initiating it was seen in 93 per cent of the cases.

The frequent finding of bile in the stomach can be explained only by duodenal reflux. It is not found constantly, it is true, it is known, however, that bile is not continuously discharged into the duodenum, but is dependent on periodic emptying of the gallbladder.<sup>16</sup> In general,

- 12 Ormer A. *Arch f d ges Physiol* 186 124, 1917
- 13 Drury D R, McMaster P D, and Rous P. *J Exper Med* 39 403 1924
- 14 Eisen P. *Radiol* 4 388, 1923
- 15 Bolton C, and Salmon R W A. *Lancet* 1 1230 1927
- 16 McMaster P D, and Elman R. *J Exper Med* 44 173, 1926

G H and Kodama S. Regulation of Flow of Bile and Pancreatic Juice in Duodenum. *Arch Int Med* 38 647 (Nov) 1926

patients suffering from intestinal obstruction is increased, and they recommended the use of an antitryptic ferment. Chenut<sup>48</sup> has examined histologically the intestinal wall in cases of simple obstruction and has observed evidence of damage to the mucosa at and above the level of obstruction. He found muscular and mucous and submucous layers thinned out. The epithelium over the intestinal villi appeared desquamated in areas.

In strangulating types of obstruction when gross evidence of damage to the intestinal wall such that the bowel is no longer viable is present, the bowel undoubtedly becomes permeable to the products of autolysis of the wall of the bowel consequent on the strangulation and to the contents within the lumen as well. When the viability of the wall of the bowel in simple obstruction is threatened by the distention of the intestine, permeation of the wall by toxins and absorption via the peritoneal cavity no doubt may also occur. As has been pointed out previously,<sup>10</sup> however, it is unusual to observe destructive changes in the wall of the bowel during simple occlusion. Distention ulcers or the gangrenous patches that occur on the antimesenteric border of the strangulated intestine are infrequently observed in simple obstruction. We have observed them frequently in closed loop obstruction with the continuity of the remainder of the tract reestablished. The tension in such a loop with both ends closed must, therefore, be much greater than in simple severance of the continuity of the bowel.

The fact that dogs with an obstruction high up in the severed gut can live for three weeks after having been given saline solution subcutaneously for a few days militates against the theory of the migration of toxins through the wall of the bowel and their absorption via the peritoneal cavity in simple obstruction. A great amount of toxin was not absorbed through the distended wall of the bowel in the animal with an enormously distended intestine which lived forty-two days following severed gut obstruction in the descending colon. The absorption from the bowel via the peritoneal cavity could also not have been great in the animals with duodenal occlusion which survived the procedure for almost three weeks after a few days of subcutaneous administration of salt solution and in which the obstructed segments were found uniformly markedly dilated.

A denial is not made of the suggestion that in simple intestinal obstruction absorption may be increased over that present in the normal bowel, but evidence of it has not been elicited in these experiments. The more rapid death when the obstruction occurs high up in the intestine, however, is not accounted for by the formation and absorption of a more potent toxin than that present when the obstruction is low down in the bowel, the more likely cause is the rapid dehydration and loss of body chlorides attending obstruction of the upper part of the intestinal tract.

reverse peristalsis is not uncommon in the small intestine, as pointed out so extensively by Alvarez,<sup>17</sup> and its infrequent visualization in the duodenum may be due to the fact that it is not being looked for and to the fact that the duodenum turns posteriorly, thus making it difficult to be seen with the fluoroscope in its entire course.

Direct evidence that pancreatic juice is regurgitated into the stomach would be furnished by the finding of pancreatic ferments in the gastric contents. This has indeed been the case. Boas<sup>18</sup> apparently was the first to make such examinations, he found the pancreatic ferments in a great many persons, including those who were normal. Trypsin, the most characteristic enzyme, present only in the pancreatic juice, was recovered from healthy stomachs nearly twenty years ago by a great many observers, particularly after the giving of a test meal of olive oil.<sup>19</sup> More recently, Rehfuess and Hawk<sup>20</sup> found it constantly in the fasting contents of the stomachs of normal persons. Iwanow,<sup>21</sup> in extensive observations on human beings, amply confirmed their observations. That trypsin may not be found when the contents are acid is due to the fact that it is destroyed in an acid medium.<sup>22</sup> Negative tests, therefore, are not conclusive. The frequent demonstration of trypsin in the stomach, on the other hand, can mean only that reflux of pancreatic juice has occurred.

The clinical applications of these observations chiefly concern the meaning of variations in gastric acidity found in real or supposed disease of the gastro-intestinal tract. The hyperacidity frequently found in cases of peptic ulcer, for example, has been ascribed to hypersecretion and the absence of, or low values for, acid in certain cases of so-called achylia to hyposecretion. From the evidence herein reported, it would seem that variations in the degree of regulation of pancreatic juice into the stomach may well be the important factor. A diminished reflux would permit the acidity to mount and account for the finding of hyperacid contents. An increased reflux, on the other hand, would so rapidly neutralize the acidity produced after a test meal that a low acidity or absence of acidity would be found. Indeed, in a recent

17 Alvarez, W. C. The Mechanics of the Digestive Tract, New York, Paul B. Hoeber, 1922.

18 Boas, J. Ztschr. f. klin. Med. 17 155, 1890.

19 Mahlenbrey, J. Zentralbl. f. d. ges. Physiol. u. Path. d. Stoffwechs. 4 643, 1909.

20 Rehfuess, M. E., and Hawk, P. B. Gastric Analysis. Interdigestive Phase or Principle Governing the Resting Stomach, J. A. M. A. 76 564 (Feb. 26) 1921. Spencer, W. H., Meyer, G. P., Rehfuess, M. E., and Hawk, P. B. Am. J. Physiol. 39 459, 1916.

21 Iwanow, W. Arch. f. Verdauungschr. 38 223, 1926.

22 Kuda, T. Biochem. Ztschr. 15 473, 1909. Deutsch, G., and Rurup, H. Deutsches Arch. f. klin. Med. 138 165, 1922.

That liver insufficiency does not play a great rôle in simple obstruction, as has been suggested,<sup>45</sup> is apparent from the injections of histamine into the mesenteric veins of dogs with intestinal obstruction, described in a previous paper. The liver of animals with intestinal obstruction still possessed the same slightly detoxifying action for histamine observed in the liver of normal animals. The presence of a high blood fibrin in animals with an obstruction in the upper part of the intestine, as observed by Haden and Orr,<sup>46</sup> is also against such an assumption.

The increase in the excretion of nitrogen in the urine could be due to a toxic action occasioned by abnormal absorption, but the same obtains in obstruction of the cervical esophagus. Is it likely that absorption plays any great rôle in the death of such an animal?

#### SUMMARY

Obstruction of the upper part of the intestine is much more serious than obstruction low down in the colon. An animal with the former type of obstruction dies sooner because dehydration and loss of chlorides occur more rapidly. Subcutaneous administration of saline to such an animal prolongs his life and obviates the alteration in blood chemistry noted in animals with duodenal obstructions to which salt solution is not given. An increased excretion of nitrogen, however, also occurs in the urine of animals with duodenal obstruction to which salt has been given. A temporary administration of saline is just as efficient in prolonging the animal's life as continued daily administration. Therefore, the virtue of the remedy cannot lie in any detoxifying mechanism. The fact that animals with gastric or duodenal fistulas die as quickly as dogs with obstructions at the same level and with the same changes in the chemistry of the blood and increase in nitrogen excretion in the urine, and the fact that the administration of saline prolongs the life of such an animal also indicate that the virtue of the drug lies in substitution therapy. Dogs with duodenal obstruction on which gastro-enterostomy has been performed can live indefinitely when given salt solution for a few days. In such an animal, the conditions are right for permanent recovery when the dehydration and the loss of the contents of the stomach incident to the obstruction have been ameliorated by the administration of saline. The animal with esophageal obstruction does not lose chlorides and fluid by vomiting, but the life of the animal can be prolonged by the administration of saline. On the same basis of loss of fluid and fixed base from the body, some alteration in the permeability of tissue is necessary to

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<sup>45</sup> Werelius. A. Is Death in High Intestinal Obstruction Due to Liver Insufficiency? *J. A. M. A.* **79** 535 (Aug. 12) 1922.

<sup>46</sup> Haden and Orr. Blood Fibrin in Upper Gastro-Intestinal Tract Obstruction. *J. Exper. Med.* **45** 427, 1927.

# THIRTY-FIFTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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(Continued from page 1126)

## MISCELLANEOUS

*Orthopedic Surgery in Sweden*—Hausser<sup>39</sup> has given an interesting account of orthopedic developments in Sweden growing out of national, social, and health insurance legislation. Sweden early recognized that it was advisable for the community to assume the responsibility of alleviating the circumstances of the poor and needy, and a comprehensive law was passed for the benefit of all who were in need of social aid. The provisions of this law include the medical care of invalids and cripples. The system of pensioning invalids, part of the socialistic national insurance scheme which has been adopted, also influences the practice of orthopedic surgery, in that it has been found expedient to cure, or at least reduce as far as possible, invalidism before the amount of disability is fixed and a pension allocated. Under the supervision of a central committee for the care of cripples, the state organized three orthopedic centers, one at Stockholm, one at Helsingfors and one at Gothenburg. Each center comprises several units besides the diagnostic and hospital sections, and includes a home for crippled children, vocational training schools, special hospitals for the care of patients with tuberculosis of the bones and joints, and three seaside sanatoriums.

*Summary of Literature Relating to Posture*—Schwartz<sup>40</sup> made a survey of 134 articles relating to posture, all of any importance that could be found in the literature. From this study he also concluded that most authors are in agreement on the following statements: 1. The

39 Hausser E D M J & Rec 125 789 (June 15) 1927  
40 Schwartz L Pub Health Rep 42 1219 (May 8) 1927

explain the death of an animal with esophageal obstruction or a rabbit with duodenal obstruction that does not vomit. In the animal with ileal or colonic obstruction the marked increase of nonprotein blood nitrogen and low values for blood chlorides are not obtained. The administration of saline in low obstruction would therefore not afford the same protection as it does to animals with duodenal obstruction.

#### CONCLUSIONS

1 The explanation of the rapidly fatal issue in dogs with obstruction in the upper part of the intestine is to be found in the rapid dehydration and loss of chlorides accompanying occlusion of this portion of the bowel.

2 The virtue of saline solution in the treatment of patients with obstruction in the upper part of the intestine does not lie in any protective or detoxifying influence, but in its value in replacing the chlorides and fluid lost.

3 Evidence was not obtained to show that dogs with simple obstruction in the upper part of the intestine died as the result of absorption of toxins from the obstructed bowel.

4 Interference with the continuity of the upper part of the intestine (occlusions or complete external fistula) gives rise to an increased nonprotein nitrogen in the blood and low blood chloride values, an increase in the excretion of nitrogen in the urine also occurs. The administration of sodium chloride prevents the increase in the nonprotein nitrogen of the blood, but the urinary excretion of nitrogen continues to be high.



biped posture of man has been evolved from the quadruped posture 2 The body has not yet fully adopted itself to the biped posture 3 There are many physical disadvantages to the erect posture, but they are outweighed by the physical and mental advantages resulting therefrom 4 Good posture can be attained by having good health, taking enough exercise to keep the muscles strong and the joints supple, and continually assuming correct postures in the daily tasks 5 Fatigue is the most frequent cause of postural deformities in the industries 6 Continuous sitting or standing in any position is fatiguing 7 Change of posture at the will of the worker is the remedy for industrial fatigue 8 Industrial furniture should be so constructed as to fit the individual worker and to allow comfortable working conditions in both the sitting and the standing postures The author's personal comments are as follows 1 There is a lack of agreement in the various definitions of standards for good posture 2 Heredity, type of build, balance of muscle strength and tone have not been given sufficient importance in establishing standards for posture 3 It has not been established that faulty posture associated with certain diseases is the cause or result of these diseases 4 There is no universally satisfactory test for physical fitness

*Loose Bodies in Joints*—In a discussion of the pathogenesis of loose bodies in joints, Platt<sup>41</sup> classified them as follows

Group 1—Diseased joints The patients have usually passed middle age and the loose bodies are multiple The causes are osteo-arthritis and Charcot joints

Group 2—Otherwise Healthy joints Included in this group are the great number of patients with "osteochondritis dissecans" of Koenig Platt discussed the various theories as to the etiology of the condition without reaching any conclusion

Group 3—Synovial Chondromas It is probable that these bodies are actually tumors from rests of cartilage cells contained in the synovial membrane The bodies are usually multiple, may become detached, and may reattach themselves

*Madelung's Deformity*—Writing on the subject of Madelung's deformity, Catterina<sup>42</sup> set down the following conclusions 1 Madelung's deformity is characterized by an abnormal curve of the radius, followed by a subluxation, more or less marked, of the ulna, and is a disease that occurs in adolescence, especially in girls 2 Such lesions must be attributed to rickets Vigorous movements, as of dorsal flexion of the hand due to special occupations, may accentuate the pre-

41 Platt, Harry Brit M J 1 947 (May 28) 1927

42 Catterina, A Chir d org di movimento 10 517 (April) 1926

# PROBABLE INFLUENCE OF PANCREATIC JUICE IN THE REGULATION OF GASTRIC ACIDITY\*

ROBERT ELMAN, M D

ST LOUIS

Drainage of the total external secretion of the pancreas, as already reported in a previous communication,<sup>1</sup> leads to increasingly severe vomiting in a few days, and, in about a week, to a fatal outcome. In the attempt to explain these symptoms of gastric irritability, a number of observations were made. The contents of the stomach were examined in most of the animals, and the behavior of gastric acidity was studied in a special way. The results will be presented in detail. They have suggested among other things that a reciprocal relationship exists between the alkaline pancreatic juice and the acid secretion of the stomach.

One aspect of this relationship has long been known, and the data herein contained adds further proof, that is, that the acid gastric juice, passed into the duodenum, is the normal stimulus of pancreatic secretion. Its discovery by Dolinsky<sup>2</sup> in Pavlov's laboratory has been amply confirmed by all subsequent observers. Others of Pavlov's pupils, notably Boldyreff,<sup>3</sup> brought forth evidence to support the idea that by reflux into the stomach the alkaline pancreatic juice neutralized and thereby regulated the level of gastric acidity. The latter hypothesis has remained more or less unconfirmed, though in the past few years much evidence in its support has accumulated. The observations herein recorded, as will be pointed out subsequently, not only seem to support this theory, but also tend to indicate that it may be an important phenomenon.

## METHODS

All observations were made on healthy adult dogs in which the total external secretion of the pancreas was being drained to the outside in a closed collecting system under aseptic conditions. This was possible by intubating the large pancreatic duct according to a method previously described<sup>1</sup>. In some dogs, provision was made for the return of the juice to the duodenum so that the secretion could be collected or reverted to the animal at will. The experiments here described were always performed during the first days of drainage and, therefore, before the onset of the severe vomiting.

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\*From the Department of Surgery, Washington University School of Medicine and Barnes Hospital

1 Elman, R., and McCaughan, J. M. J. Exper. Med. **45** 561, 1927

2 Dolinsky, J. L. Diss., St. Petersburg, 1894

3 Boldyreff, W. Ergebn. d. Physiol. **11** 121, 1911

metatarsophalangeal joint which Mueller<sup>48</sup> previously described he added the report of three more. The clinical signs which he noticed were pain, tenderness and moderate swelling under the affected area. Roentgen-ray examination showed the medial sesamoid bone divided in from two to three fragments. The patients were from 20 to 30 years old. The cause, according to the author, was occupational strain. Histologic examination revealed necrotic areas in the bony tissue but not in the marrow. Mechanical irritation is supposed to have resulted in fragmentation of the necrotic bone. The treatment is stated to be support of the foot in patients with slight symptoms and operative excision when the symptoms are severe.

# BONE, JOINT, AND TENDON SURGERY

*Spinal Anesthesia in Orthopedic Surgery*—Peabody<sup>49</sup> employed spinal anesthesia in 100 orthopedic operations and feels that it is particularly adapted to this class of cases. He found that it may be applied successfully in all procedures below the level of the dorsal spine, and his experience supplements that of others in establishing that it is a safe form of anesthesia.

*Pneumatic Hammer for Operation on the Bone*—Pitkin<sup>50</sup> described a pneumatic hammer for use in bone surgery. It is an adaptation of the Boyer U-type hammer manufactured by the Chicago Pneumatic Tool Company. The author described this hammer as a simple tool, sturdy, easily cared for, and safe.

*A Pendulating Bone Saw*—Not satisfied with the commonly used bone saws, Von Baeyer<sup>51</sup> constructed a pendulating saw. The ordinary rotary electric saw cannot be used in deep incisions unless a large blade is attached, and this represents a decided danger for the soft tissues. The author's saw is constructed with two swinging saw blades which work in different directions. They are driven in opposite directions with great rapidity and slight vibration by an electric motor. It is stated that an average sized long bone can be cut through in thirty seconds with this instrument.

*Operative Splitting of the Vertebral Column in Pott's Disease*—Lange<sup>52</sup> reported his experience with fifty-two patients with Pott's disease in whom he performed operative splitting of the spine by introducing celluloid splints of from 5 to 10 mm. in diameter and from 10 to 30 cm. in length. As he described it, his technique is to expose the spinous

- 48 Mueller, W. Beitr. z. klin. Chir. 138 494, 1926
- 49 Peabody, C. W. J. Bone & Joint Surg. 9 450 (July) 1927
- 50 Pitkin, H. C. J. Bone & Joint Surg. 9 505 (July) 1927
- 51 Von Baeyer, H. Zentralbl. f. Chir. 54 2394, 1927
- 52 Lange, Fritz. Surg. Gynec. Obst. 44 668 (May) 1927

The contents of the stomach were obtained with a small rubber tube connected at one end with a small perforated metal bulb such as is used for duodenal drainage. The animal was placed in a Pavlov frame while aspirations were performed. The acidity of the contents of the stomach were determined by titration with tenth normal sodium hydroxide with dimethyl-amino-azobenzene (Toepfer's reagent) as the end point for "free", and phenolphthalein for "total", acid. All samples were centrifugalized, since most of them contained a good deal of debris, particularly those removed from the fasting stomach. Only the clear fluid thus obtained was used in titrations.

To study the behavior of gastric acidity, a "test meal" of 200 cc of 0.5 per cent hydrochloric acid was used as originally devised by Boldyreff.<sup>4</sup> The solution was deliberately introduced by gavage, and specimens were aspirated every ten or fifteen minutes thereafter till the stomach was empty. Animals were deprived of food for from four to six hours, as a rule, and the contents of the stomach were emptied before the experiment was begun.

These experiments afforded opportunity, at the same time, to measure the effect of gastric acidity on the secretion of the pancreas. The collecting tube draining the gland was connected with a sterile graduate, and the amounts of fluid flowing were recorded at regular intervals, both before and after the acid was given.

#### EXPERIMENTAL OBSERVATIONS

*The Acid Stimulus to the Flow of Pancreatic Juice*—Fractional readings of the secretion of pancreatic juice following the introduction of 0.5 per cent hydrochloric acid into the stomach revealed an immediate and marked augmentation in the rate of flow. In the instance represented in chart 1, typical of a number of identical experiments, 51 cc of clear sterile secretion was collected during the course of one hour after the acid was given, or nearly three times the hourly average of the entire twenty-four hour output. Though this confirms the observations of other workers, I believe that my experiments are the first performed on unanesthetized animals yielding sterile juice from the entire pancreas and must, therefore, more closely represent the normal conditions.

*Failure of Acid Neutralization during Drainage of Pancreatic Juice*—Normally, acid solutions introduced into the stomachs of healthy dogs,<sup>4</sup> as well as healthy human beings,<sup>5</sup> are promptly and completely neutralized. This progressive lowering of acidity did not occur in animals in which the total pancreatic juice was flowing to the outside. It remained high, so that aside from a slight drop at first, the titrated acidity (against phenolphthalein) of the final sample was nearly the same as that of the first one. Twelve experiments were performed on eight different animals, and the results were the same. The curves in chart 2 represent an instance in a dog provided with an "altercursive" or double intubation which enables juice to drain to the outside or to

4 Boldyreff, W. Quart J Exper Physiol 8 1, 1914

5 Boldyreff (footnote 4) Apperly, F. L., and Cameron, G. Med J Australia 1 521, 1923

processes and separate the muscles from their sides down to the vertebral arches. "Each of the exposed spinous processes is perforated at the upper half and a loop of silk thread (no 12) is carried through the hole. Through a second hole, drilled a little below or through the interspinous ligaments, the same loop of thread is returned to the other side, leaving thus a U-shaped loop of double thread on one side and the four open ends on the other. A celluloid splint which has been fitted exactly to the curve of the gibbus is inserted in the loop and another similar splint is placed on the other side of the spinous processes. The latter splint now being grasped between the free ends of the thread with a firm tension is securely tied to the spinous processes with a knot." The splints are fixed in similar fashion to each of the spinous processes. "They are then carefully covered up with muscles and fascia and sutured in the ordinary way with silk no 6." A plaster of paris dressing is used for six weeks and then a corset is worn for two years. Since 1924 he has used one splint of rust-proof steel and one of celluloid. In reference to Albee's and Henle's modifications Lange said that he preferred his own method, as it involved less danger of fracture of the splint, and the bone splint requires a prolonged dressing with plaster of paris and a stay in bed of six months or more.

[ED NOTE—Either of the methods commonly employed for obtaining bony fusion of the spine, Albee's or Hibbs', seems so far superior to Lange's method of securing fixation by means of celluloid splints that we consider it unnecessary to point out the advantages of the former or the disadvantages of the latter.]

*Transplantation of Trapezius Muscle for Paralysis of the Abductors of the Shoulder*—Mayer<sup>53</sup> described a method of transplantation of the trapezius muscle for paralysis of the abductors of the shoulder. It consists, briefly, in detaching the trapezius muscle from its bony insertion, lengthening it by means of an artificial tendon constructed of fascia lata, and suturing this tendon to the humerus near the deltoid insertion. To secure a satisfactory result it is necessary that the trapezius, the serratus magnus, and the pectoralis major, or the coracobrachialis or the biceps be present and active. The author reported the results in six patients: one failure, one poor result, and four gratifying results.

*Habitual Dislocation of the Shoulder*—Still another operative procedure has been added by Carrell<sup>54</sup> to the long list of those previously described for the relief of habitual dislocation of the shoulder. The author's operation is stated to combine the principles of the suspension and reefing procedures. The suspension element is accomplished

53 Mayer, L. J Bone & Joint Surg 9 412 (July) 1927

54 Carrell, W B Habitual Dislocation of Shoulder, J A M A 89 948 (Sept 17) 1927

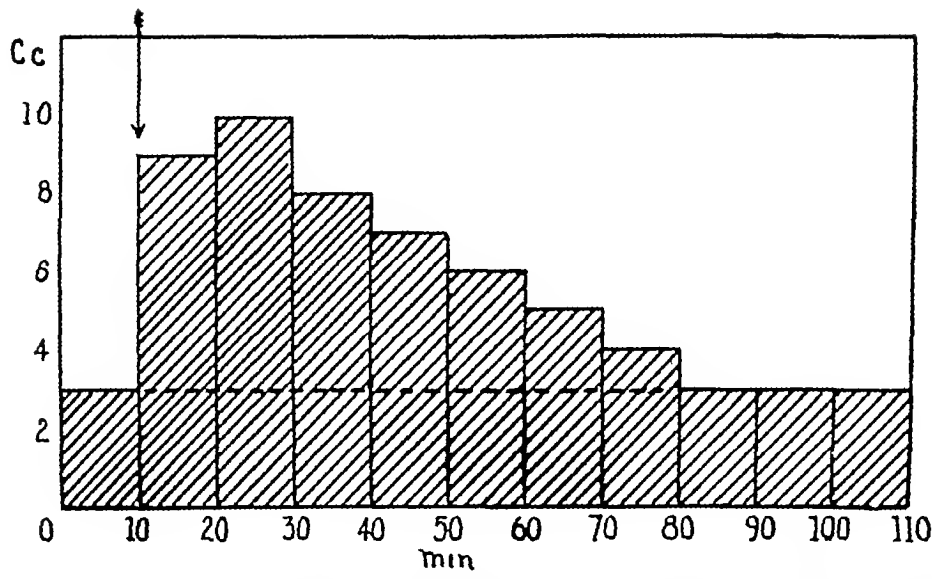


Chart 1—The acid stimulus to the flow of pancreatic juice is shown by the prompt increase in the rate of secretion from an intubated dog following the giving of 200 cc of 0.5 per cent hydrochloric acid by gavage (indicated by the arrow). The normal rate of flow of 3 cc for each ten minutes increased to 9 and then to 10 cc, and gradually dropped back to the normal rate after eighty minutes. The dog weighed 10 Kg.

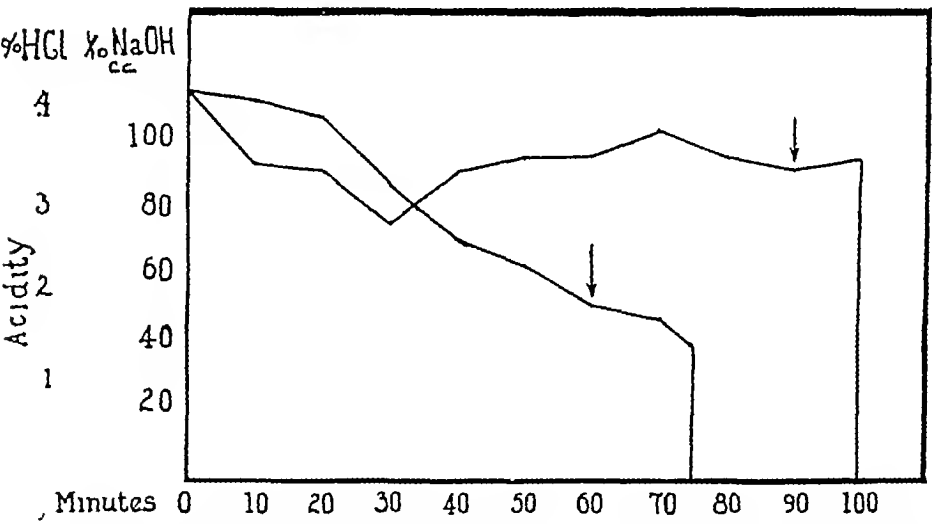


Chart 2—The failure of acid neutralization in the stomach after the giving of 200 cc of 0.5 per cent hydrochloric acid by gavage to a dog draining the entire pancreatic juice is shown in the upper curve. The titrations for "total" acid in successive aspirations remained high even after one and one-half hours. By contrast the prompt neutralization is shown in the lower curve of the same experiment in the same dog, but at a time when pancreatic juice was flowing back to the duodenum. The difference of twenty-five minutes in emptying time should also be noted (see text). The lower arrow indicates pancreatic juice flowing to the duodenum, the other arrow indicates pancreatic juice flowing to the outside.

by using the tendon of the biceps, to which is fastened a long strip of fascia. This is then passed under the neck by a special instrument, penetrating the capsule in two places, and is secured in a drill hole in the acromion. This gives a slinglike action and anchors the head in the glenoid as well as to the acromion. The reefing feature has the advantage of plicating a heavy fascial band through the weak portion of the capsule, and the resulting fibrosis should leave a thick band encircling the neck and continuous with the suspension band. The operation was performed on four patients, and unsatisfactory results have not yet been seen. Ill effects from changing the biceps origin have not been noted.

[ED. NOTE—It seems to us that the operation described does not offer any particular advantage over the method of direct fixation of the humeral head to the acromion by a fascial band. It appears considerably more complicated.]

*Operations on the Upper Extremity*—Steindler<sup>55</sup> analyzed the kinetics of the upper extremity and the various operative measures employed for the relief of paralysis of the shoulder, of the elbow, and of the wrist. Arthrodesis of the shoulder was performed in sixty-five patients because of paralysis of the deltoid. On the whole, the results were satisfactory, but not uniformly so. He found that the optimum functional position varied in children and adults, in adults, from 60 to 70 degrees. The author's operation for relief of paralysis of the flexor muscles of the elbow was performed on thirty patients, and the results have been satisfactory. The operation consisted of transplanting the common origin of the pronator teres, flexor carpi ulnaris, palmaris longus, and flexor carpi radialis muscles to a point higher up on the humerus. Forty-two operations were performed for relief of pronation contracture, mostly of the spastic type. The operation consisted of a resection of the pronator teres or pronator quadratus, and tendon transplantation of the pronator and flexor carpi ulnaris to the dorsum of the forearm. Paralysis of the wrist were treated by the operation of arthrodesis in fifty-four patients, and by tendon transplantation in thirty-four patients.

[ED. NOTE—Steindler is a careful student and has had a great deal of experience in the treatment of paralytic conditions of the upper extremity which entitles his opinion to respect.]

*Loop Operation for Paralysis of Adductors of Thumb*—A loop operation for relief of paralysis of the adductor muscles of the thumb has been originated by Mayer.<sup>56</sup> This operation retains the essential features of the so-called pulley operation of Bunnell. It consists of passing

<sup>55</sup> Steindler, A. J. Bone & Joint Surg. 9:404 (July) 1927.  
<sup>56</sup> Mayer, L. Am. J. Surg. 2:456 (May) 1927.

flow back to the duodenum at will<sup>1</sup> The lower curve shows the normal drop in the acidity of the solution introduced into the stomach at a time when pancreatic juice was flowing back to the duodenum, the upper one, the absence of neutralization when it was draining to the outside

The experiments of Bolyreff<sup>2</sup> and of Migay<sup>6</sup> may well be referred to at this point These authors did not find any lowering in the acidity of hydrochloric acid solutions given dogs after ligation of the pancreatic ducts or after occlusion of the pylorus When the common bile duct or lower end of the esophagus was obstructed, neutralization proceeded normally They concluded from this that neither bile nor swallowed saliva are responsible for the phenomenon, but rather the reflux of pancreatic juice into the stomach

It is of special interest to note the behavior of "free" and of "combined" acid in these experiments, as shown in chart 3, which represents a typical instance Though the former value fell, the latter rose *pari passu*, so that the "total" acid remained the same In the normal, combined acid was not found,

*Titration of the Clear Fluid Obtained After Centrifugation of the Contents of a Stomach Removed from Fasting Dogs Draining Pancreatic Juice Showing High Combined and Total Acid in Contrast to Those Removed from Dogs in Which the Juice was Flowing Back to the Duodenum*

Dog	Hours After Food	Day of Drainage	Free Acid	Combined Acid	Total Acid
51	8	4	40	103	143
54	9	2	24	88	112
63	6	1	88	90	128
63	36	3	0	78	78
50	4	2	18	64	82
53	6	2	10	86	96
52	18	2	0	40	40
59	6	{ 'Altercursive' fistula with pancreatic juice flowing back to the duodenum }	36	16	52
59	36		28	8	36
53	4		32	12	44

as the total and free acid were always the same, the fall in acidity affecting each equally This phenomenon may well be explained by the probable buffer action of the large amounts of intestinal contents regurgitated into the stomachs of these dogs which lose their total pancreatic juice The samples in the normal, on the contrary, were always clear The significance of this observation will be discussed

*The High Acidity of the Fasting Contents of Dogs Draining the Total Juice*—The contents of the stomach obtained from dogs after one or more days of drainage showed a much higher "total" acid than normal, in a few cases, it was three times as great (table) These specimens, too, showed a high value for the "combined" acid and contained a considerable amount of intestinal contents, as already mentioned

*The Regurgitation of Intestinal Contents into the Stomach*—In every instance in which the contents of the stomach were aspirated during the

6 Migay, F, quoted by Babkin, B P Diss, St Petersburg, 1909, Die äussere Sekretion der Verdauungstruse, 1914, p 382



the subimus tendon of the ring finger through a loop formed by uniting the two ends of the free transplant of the subimus tendon of the middle finger. The free end of the subimus tendon of the ring finger is carried diagonally across the palm and drawn through a drill hole in the base of the proximal phalanx of the thumb. In the five patients on whom the operation was performed, there is excellent opposing action of the thumb and the usefulness of the hand has been much improved. The transplanted tendon can be felt to glide freely through the pulley loop.

*Reconstruction of the Crucial Ligaments of the Knee*—Horan<sup>57</sup> reported the results of reconstruction of the anterior crucial and internal lateral ligaments of the knee in eleven patients operated on by Alwyn Smith. The latter's modification of Hey Groves' operation (fascial substitution) was employed. All the patients were pensioners, and for this reason their responses were somewhat cautious, but with three exceptions good knees were reported. In one patient an arthrodesis was performed five years after the original operation, and during this procedure a strong viable crucial ligament was found. The author concluded that the operation results in a joint capable of withstanding the stress and strain to which it is subjected in the course of an average life.

*Arthrodesis of the Ankle*—For the condition of complete paralysis of the foot Straub<sup>58</sup> advocates the operation of pseudarthrosis of the ankle, including the tibio-astragal, the subastragal, the calcaneo-cuboid, and the astragaloscaphoid joints. To make the astragalus completely fill the space between the malleoli he splits the astragalus in the mid-sagittal plane, after removing the cartilaginous surfaces, and inserts a disk of bone cut from the anterior pole of the head of the astragalus. This separates the two halves of the astragalus and forces the outer surfaces of the halves against the inner surfaces of the malleoli.

*Etiology of Claw Foot*—Royce<sup>59</sup> made a study of the etiology of the claw foot and concluded that the primary condition is a weakness of the gastrocnemius muscle, with a compensatory increase in the function of the tibialis posterior muscle. Proceeding on this theory, he suggested that the logical treatment is transplantation of the tibialis posterior tendon into the gastrocnemius muscle. He performed this operation on nine patients, with satisfactory results.

*Reproduction of a Metacarpal Bone by a Bone Graft*—Following excision of the entire fifth metacarpal bone Fowler<sup>60</sup> succeeded in replacing it by grafting an autogenous transplant from the tibia. The

57 Horan, Maurice Brit J Surg 14 569 (April) 1927  
58 Straub, G F Surg Gynec Obst 44 675 (May) 1927  
59 Royce, N D J Bone & Joint Surg 9 465 (July) 1927  
60 Fowler, Andrew Brit J Surg 14 675 (April) 1927

drainage of the total pancreatic juice, a good deal of admixed material was found. When drainage had occurred for three or four days, the specimen was thick and brownish, and by its fecal odor it betrayed its origin in the lower ileum. Autopsy in each case showed an intact gastro-intestinal tract without evidence of gastrocolic or ileogastric fistula. It was obvious that the material in the stomach was regurgitated intestinal contents, such as are never found in the stomach under normal conditions. Centrifugalization always yielded three layers. The upper layer was grayish and proved to be neutral fat, the lower one was dark brown or black, its nature was undetermined, and there was a more or less clear fluid between the two. Titration of this fluid always showed a high content of acid.

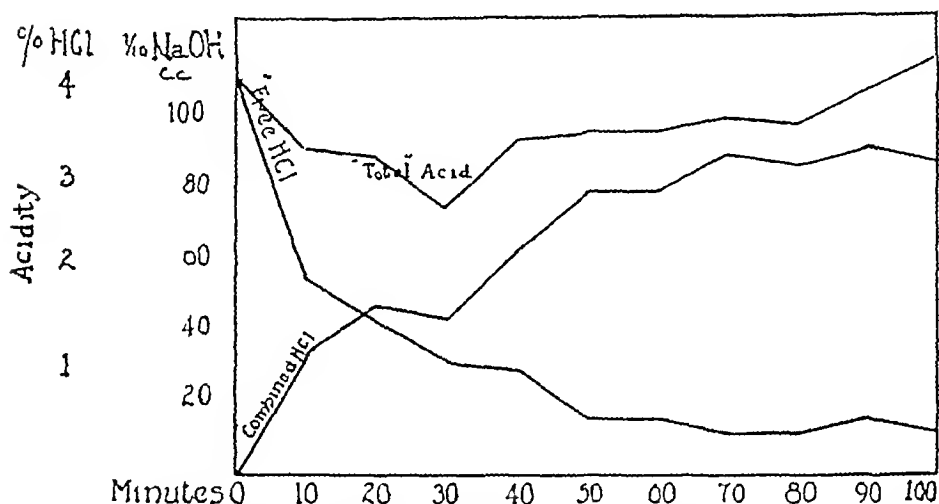


Chart 3—The behavior of "free" and "combined" acid in titration of aspirated samples after the giving of 200 cc of 0.5 per cent of hydrochloric acid solution to a dog draining the total pancreatic juice. After the free acid decreased, the combined acid increased so that the "total" acid was always the same. The aspirated samples always contained much regurgitated intestinal contents which probably accounted for this (see text).

#### COMMENT

The observations herein recorded throw considerable light on the nature of the severe gastro-intestinal upset which follows drainage of the total pancreatic secretion. In brief, they show that the contents of the stomach of such animals are abnormally acid, and, moreover, that there is a failure of neutralization to occur when acid solutions are introduced into their stomachs, though an intense flow of pancreatic juice is always provoked thereby. Finally, the constant finding of intestinal contents in the stomach of these animals shows that regurgitation occurred regularly.

The first inference from these observations was that I was dealing with a condition whereby some mechanism for the regulation of gastric

distal end of the graft was rounded and its proximal end implanted firmly in the carpus. Now after two and one-half years, he reports that nearly perfect function was present.

#### FRACTURES

*Metal Aids in the Treatment of Fractures*—Rossi,<sup>61</sup> from a study

of twenty-nine patients with fractures of the long bones, treated by internal metal fixation, drew the following conclusions: 1. In compound fractures of long bones, osteosynthesis with metallic means of direct fixation of the fragments furnishes, in many cases, a useful and necessary accompaniment either directly or after an immediate and careful cleansing of the wound. Open postoperative treatment of the wounds of compound fractures, if well immobilized, is not incompatible with the presence of metallic material. 2. When in simple fractures of long bones the roentgenograms reveal that the ordinary methods of reduction and fixation are not likely to obtain satisfactory reposition of the bones, early osteosynthesis represents the only method of treatment which is capable of giving perfect correction. Since the purpose of osteosynthesis is to secure exact temporary retention of the fragments during the period of consolidation, it must be strong enough to overcome the action of the muscles. The method of internal fixation should be simple, and capable of application with simple technique. 3. In the choice of the means of internal fixation, good judgment must be exercised. The site and accessibility of the fracture should be considered and the advisability of leaving the means of synthesis in the tissues. 4. While in compound fractures as well as in simple fractures foreign material such as metallic wire may be left in the tissues, it is necessary to remove the plates in compound fractures, and it is better to remove them when the consolidation is satisfactory in subcutaneous fractures, especially in sites like the tibia.

*Nerve Injuries Complicating Colles' Fracture*—Nerve injuries com-

plicating Colles' fracture are generally considered uncommon, but Turner<sup>62</sup> expressed the opinion that this is not the case. He found evidence of nerve involvement in several patients and was led to the belief that only on this basis can the so-called trophoneuroses of the hand that occasionally develop after Colles' fracture be explained. The author's views may be summarized as follows. The dorsal branch of the ulnar nerve lies over the ulnar head and often comes in close approximation to a fracture there. At the same level, or more distalward, lies the volar branch of the ulnar. The median nerve passes through the same region, but it is usually separated from the fracture site by the flexor pollicis longus and

61 Rossi, Aurelio. Chir d org di Movimento 10 486 (April) 1926  
62 Turner, H. Arch f klin Chir 128 422, 1924

acidity was interfered with, and the second one, that the alkaline pancreatic juice was responsible. The intense regurgitation of intestinal contents into the stomach, contents even from the lower part of the ileum, pointed to an attempt on the part of the body to compensate for the missing pancreatic juice, indeed, by its buffer action, it did exert some neutralizing effect (chart 3). Analysis of the evidence of others, finally seemed also to point to the existence of this mechanism and to its importance in the relationship between stomach and duodenum, both normally and in certain pathologic conditions.

That the level of gastric acidity is actually regulated by some neutralizing agent rather than by variations in the secretory activity of the gastric glands is based on the fact that pure gastric juice is always secreted at a much higher acidity than is ordinarily found in the contents of the stomach even after a test meal. Pavlov was the first to maintain, on the basis of his own observations, that the gastric glands secrete a juice of a constant and rather high acidity of about 0.5 per cent hydrochloric acid, or, in terms of titration values, of 140.<sup>7</sup> More recently, Carlson,<sup>8</sup> though questioning the truth of Pavlov's contention, in observing two patients with esophageal stricture and gastric fistula found that the actively secreted juice is always of a constant acidity close to 0.5 per cent hydrochloric acid. Rehfuess and Hawk reported evidence to show that human beings secrete gastric juice of a constant and high acidity,<sup>9</sup> and Hollander,<sup>10</sup> by experimentation on dogs, has shown that the actively flowing secretion from a Pavlov pouch is of a high acidity which after the injection of histamine equals a  $p_H$  of 0.92, or greater than 0.5 per cent hydrochloric acid. The much lower figures obtained in normal stomach contents must obviously be due to the existence of some neutralizing mechanism. Such a mechanism, furthermore, has been strikingly demonstrated by Kahn and Yaure.<sup>11</sup> These authors, using  $p_H$  as a measure of acidity, gave test meals to dogs with a Pavlov pouch and simultaneously studied the contents of the main stomach as well as the pure juice flowing from the isolated pouch. Whereas the former varied considerably and never was more acid than  $p_H$  1.9, the pure juice was secreted at the high and constant acidity of  $p_H$  1.1.

This regulation may occur, of course, by the diluting action of swallowed saliva, mucus, bile or pyloric secretions, and this mechanism

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7 Pavlov, J. P. *The work of the Digestive Glands*, London: C. Griffin & Company, 1910, p. 32.

8 Carlson, A. J. *Am J Physiol* **33**: 248, 1915.

9 Rehfuess, M. E., and Hawk, P. B. *Gastro-Intestinal Studies*. *J. A. M. A.* **63**: 2088 (Dec. 12) 1914.

10 Hollander, F. *Proc. Am. Soc. Biol. Chem.*, *J. Biol. Chem.* **74**: 23, 1927.

11 Kahn, J., and Yaure, G. *Arch. f. d. ges. Physiol.* **206**: 119, 1924.

the pronator quadratus muscles. The volar interosseous nerve runs more deeply and is usually in no danger of injury. The radial nerve may sometimes be injured, but the dorsal interosseous nerve is least favorably situated to escape injury. It lies in direct contact with the dorsal surface of the distal end of the radius. Careful study in the first few days of each patient with Colles' fracture will, according to the author, often reveal evidence of a nerve injury. The usual signs are excessive perspiration in the palm, hyperesthesia on the palmar side of the carpal bones, hyperesthesia of the thenar eminence, and pain over the ulnar nerve distribution, particularly when the ulnar styloid has been torn off. Bruising or overstretching are considered common, but are overlooked because the attention of the surgeon is focused on the change in the bone. The most serious changes occur in injuries of the dorsal interosseous nerve. Here after a few days, sometimes only after a week or more, a hard edema appears on the dorsum of the hand, extending to the middle third of the forearm and distalward to the second phalanges of the four fingers. The skin is glossy and usually reddened. Stiffness of the fingers soon follows, with limitation of motion both actively and passively. If one attempts motion with force, there is sharp pain in the fingers and forearm. An extension contracture of the fingers develops with slight flexion at the proximal interphalangeal joints. Motion also becomes decreased at the wrist joint. Later an actual swelling of the proximal interphalangeal joints may develop. The condition remains indefinitely without any change. Roentgen-ray examination of the hand shows increased radiability and haziness of the lower end of the radius, carpal bones, and metacarpal bones. The changes are more marked in the third and fourth metacarpal bones, and less in the second and fifth, and there is not any change in the first metacarpal bone. The changes are seen to be less marked as the examination proceeds up the forearm. The essential changes are osteoporosis and a disintegration of the internal architecture of the bone. Two cases are reported in which the changes mentioned occurred. In the second case an exploratory operation was performed on the dorsal interosseous nerve. The nerve in the region of injury was found to be somewhat spindle-shaped and congested. A slight improvement followed the exploratory operation, with less edema and less stiffness of the fingers. The author concluded that this condition is a trophoneurosis produced originally by trauma and attributable to an injury of the dorsal interosseous nerve. He added as proof three more cases in each of which the patient was bitten by a cat over the course of the dorsal interosseous nerve, and in which the same neurologic disturbances occurred as in the cases of Colles' fracture. The author did not suggest any treatment for the condition, although slight improvement did occur in one case following operation.



100 diastolic) and cardiac hypertrophy. None of these factors, however, except the anemia, can be said to have influenced the hyperthyroidism other than indirectly. These five patients, however, were suffering from conditions which placed the heart under a continuous abnormal strain. Of the eight cases, six were classed by Rienhoff as typical instances of exophthalmic hypertrophy, although the presence of a capsule had influenced the pathologic laboratory to designate them as mixed colloid and fetal adenomas. The other two patients showed more than average hypertrophy and hyperplasia.

Of the ten patients who were given iodine in the hospital, three showed marked improvement, three slight improvement and four none. Two of the patients who were not helped by iodine died, one, whose basal metabolic rate was 60 per cent above normal, had marked anemia (hemoglobin content 55 per cent, red blood cell count 3,068,000), blood pressure of 170 systolic and 60 diastolic and a large cystic goiter in which cellular hypertrophy and hyperplasia of the small acinar type were demonstrable at operation, the other, whose basal metabolic rate was 40 and 37 per cent above normal, had auricular fibrillation and a goiter of twenty-four years' duration, which showed typical cellular hypertrophy and hyperplasia with areas of degeneration. One of the patients who was not benefited by iodine became restless and had a much higher basal metabolic rate, probably as a result of psychic disturbance, in the other patient, the basal metabolic rate rose from 25 to 31 per cent above normal in ten days, and the iodine was discontinued. The three patients who improved markedly under treatment with iodine showed characteristic cellular hypertrophy and hyperplasia which had undergone an iodine remission. In two of the three patients who showed only slight improvement under treatment with iodine, encapsulated areas of cellular hypertrophy and hyperplasia were demonstrated. The effect of iodine was much less striking and less frequent in the older group than in the younger group.

The average increase in the basal metabolic rate was 39.5 per cent above normal, the average blood pressure was 162 systolic and 80 diastolic.

In the older group an appreciable secondary anemia was not uncommon, the average hemoglobin content being 66 per cent. This factor serves<sup>3</sup> at least to increase the load of the heart as well as to raise the basal metabolic rate<sup>4</sup>.

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<sup>3</sup> Blalock, Alfred, and Harrison, Tinsley R. Unpublished Observations on the Cardiac Output in Anaemia, quoted by Harrison and Leonard. *J Clin Investigation* **3** 1, 1926.

<sup>4</sup> Tompkins, E. H., Brittingham, H. H., and Drinker, C. K. Basal Metabolism in Anaemia, *Arch Int Med* **23** 441 (April) 1919.

[ED NOTE—The article by Turner was published in 1924, but was overlooked at that time and so not included in the Report of Progress in Orthopedic Surgery. Only recently was our attention called to it, but it appeared significant, and for this reason it is abstracted in this report. We have observed several patients who unaccountably developed painful stiff hands after Colles' fracture, and Turner's theory affords a plausible explanation.]

*Late Results of Fractures of Long Bones*—Walker<sup>63</sup> has continued with his studies of the late results of gunshot and other fractures among the American combatants in the World War. He reviewed the results in 4,647 fractures of the femur. He compared the results in veterans who applied to the bureau for relief twelve, eighteen, twenty-four, thirty, and thirty-eight months after injury. After a period of four years, the examination showed an improvement in disability rating of 86 per cent in the twelve months group, 77 per cent in the eighteen months group, 62 per cent in the twenty-four months group, 45 per cent in the thirty months group, and only 14 per cent in the thirty-six months group.

*Epiphyseal Separation of the Ischium*—Schoolfield<sup>64</sup> described the rare case of a patient with epiphyseal separation of the ischium. Roentgen-ray examination showed an inward displacement with considerable encroachment on the pelvic cavity, the ilium and pubes apparently remaining in normal relationship. There was a defect in the acetabulum. The head and neck of the femur showed changes characteristic of Legg-Calve's disease. A perfect reduction was finally obtained following two manipulations and fixation of the hip in a position of wide abduction.

*Fractures of the Knee*—Zanoli<sup>65</sup> made a study of fractures in the region of the knee, excluding fractures of the patella, using the material of the Rizzoli Institute. Between the years 1899 and 1922, thirty-four patients with such fractures were treated of a total of 1,864 fractures, thus making a proportion of 1.23 per cent. Interarticular fractures of both the lower end of the femur and the upper end of the tibia were included. From a study of the results the writer concluded that conservative treatment, using the traction apparatus of Zuppinger until replacement of the fragments is obtained and then immobilization in a plaster casing, is the method of choice.

[ED NOTE—We do not know of any more difficult fracture problem than that represented by some of the interarticular fractures of the upper end of the tibia. The entire joint surface may be disrupted, and

63 Walker, J. B. U. S. Vet. Bur. M. Bull. 3: 651 (July) 1927.

64 Schoolfield, B. L. J. Bone & Joint Surg. 9: 498 (July) 1927.

65 Zanoli, R. Chir. d'org. di Movimento 10: 463 (April) 1926.



oped auricular fibrillation with the thyrotoxicosis. This was the only case in the younger group in which auricular fibrillation was noted, whereas in the older patients, whose hearts were less able to stand the strain, fibrillation occurred in eight cases. The fact that the cardiac symptoms always cleared up, or at least were greatly ameliorated, after thyroidectomy is, apparently, an argument against any cardiac damage resulting from the thyrotoxicosis. At any rate, it proves that the condition of these hearts (in this series all to be found in the older group) may change from auricular fibrillation and myocardial insufficiency to normal rhythm and compensation when the metabolism has been lowered and presumably the thyrotoxicosis has been removed.

Christian<sup>9</sup> cites two instances of cardiac decompensation which occurred when the basal metabolic rate in long-standing cases of myxedema was brought up toward normal by the use of desiccated thyroid gland. The heart in these cases was able to function satisfactorily on a low plane of metabolic activity, but was unable to stand the added burden brought about by an increase in the metabolic rate. In like manner one may explain the satisfactory therapeutic results of subtotal thyroidectomy reported by Hamilton<sup>10</sup> in two cases of cardiac decompensation with nodular goiter, without hyperthyroidism. In these cases, compensation was established when, presumably, the metabolic rate was lowered from normal to subnormal, and the question of thyrotoxicosis did not enter in.

Robinson and Burwell,<sup>11</sup> studying a case of hyperthyroidism, find the cardiac output greatly increased, and believe this to be an evidence of abnormal heart strain. Similar observations are reported by Liljestrand and Stenstrom<sup>12</sup> who report observations on eleven cases of exophthalmic goiter in which there was a cardiac output of 80 per cent above normal (female) and 100 per cent above normal (male). Harrison and Leonard<sup>13</sup> believe, from their study of cardiac decompensation in dogs, that this condition is associated with an increased cardiac output, and Robinson<sup>14</sup> reports confirmatory observations in

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9 Christian, H. A. *The Heart and Its Management in Myxedema*, Rhode Island M. J. **8** 109, 1925.

10 Hamilton, Burton E. *The Heart in Toxic Thyroid States*, S. Clin. N. Amer. **4** 1411, 1924.

11 Robinson, G. C., and Burwell, C. S. Personal communications, quoted by Harrison, T. R., and Leonard, B. W. *J. Clin. Investigation* **3** 1, 1926.

12 Liljestrand, G., and Stenstrom, N. *Circulation in Exophthalmic Goiter*, *Acta med. Scandinav.* **63** 99, 1925, abstr., *J. A. M. A.* **86** 456 (Feb. 6) 1926.

13 Harrison, T. R., and Leonard, B. W. *The Effect of Digitalis on the Cardiac Output of Dogs and Its Bearing on the Action of the Drug in Heart Disease*, *J. Clin. Investigation* **3** 1, 1926.

14 Robinson, G. C. *The Disturbances of Cardiac Function Leading to Heart Failure*, *South M. J.* **20** 222, 1926.

injuries of the semilunar cartilages and of the crucial and lateral ligaments are frequent accompaniments. The only chance of restoring function in such a knee lies in early operative treatment. There is such wide variation in the damage caused by these fractures that it is impossible with fairness to group them in one class and conclude, as the author of the foregoing article has done, that nonoperative treatment is the method of choice.]

## RESEARCH

*Influence of Diet on Healing of Wounds*—Herrmannsdorfer,<sup>66</sup> who in collaboration with Sauerbruch previously studied the effects of diet on patients with surgical tuberculosis, has now gathered together his observations bearing on the effects of diet on wounds and infections. He found important differences between the metabolism of healthy persons and that of persons with infected wounds. The reaction of infected wounds is acid, and the more severe the infection the greater the acidity. The alkali reserves of the blood are lowered. He stated that it is possible by suitable diet to influence the acidity of the wound and that this can be demonstrated. With an acid diet the weight of the body is in balance, the wound shrinks, the secretion decreases, and the bacteria diminish, in both variety and number. On the other hand, with an alkaline diet the weight of the body increases and the appearance of the wound changes for the worse. The granulations swell, the wound secretion becomes greater in amount, a pseudodiphtheritic membrane spreads over the surface, and the bacteria are increased in number and in variety. The writer expressed the belief that the experiments clearly show that the living tissues are subject to great variation in chemical composition and that these changes have an influence in determining whether bacteria will find them favorable or unfavorable culture mediums.

[ED. NOTE.—We report this article with reserve, hoping that it may stimulate others to repeat the experiments and either confirm or disprove Herrmannsdorfer's observations.]

*Joint Fluid Ferments*—Abderhalden and others have shown that the juices of certain organs have specific reactions resembling those of ferments in that they act only on peptones obtained from those organs. Hempel<sup>67</sup> tested synovial fluid on joint cartilage, using Abderhalden's microtechnic. In six of twenty-two patients specific ferments were demonstrated, in seven patients the results were negative, and in the remaining patients the joint fluid was not of a character to permit optical examination. In four of the six positive tests, the cartilage was distinctly affected. The reaction is said to be so exact that a lesion of

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66 Herrmannsdorfer, A. *Deutsche Ztschr. f. Chir.* 200:534, 1927.

67 Hempel, C. *Zentralbl. f. Chir.* 54:2377, 1927.

## CONCLUSIONS

1 In a series of thirty-two cases designated as instances of nodular goiter with hyperthyroidism, sections from the gland in every instance revealed areas of hypertrophy and hyperplasia of the thyroid epithelium

2 Patients in the age group below 45 years show pathologic changes closely simulating those of exophthalmic goiter, and their disease may be classified as mild, pure hyperthyroidism

3 Patients in the age group above 45 years nearly all present morbid conditions such as heart failure, hypertension, obesity or anemia, which, when augmented by more or less slight hyperthyroidism, present a serious clinical picture

4 When one considers the various factors which combine to produce the clinical picture, a close parallelism is seen between the degree of hypertrophy and hyperplasia of the thyroid epithelium and that of thyrotoxicosis

5 These cases of nodular goiter with hyperthyroidism seem to differ from cases of exophthalmic goiter chiefly in the degree of thyrotoxicosis, and occur mainly in elderly persons who are suffering also from other conditions which disturb their circulatory mechanism

6 These facts seem to be in accord with Rienhoff's hypothesis, that 92 per cent of nodules in the thyroid gland are the result of a long-standing or frequently recurring overactivity of the thyroid gland

the cartilage which is invisible macroscopically may give a positive result Hempel also pointed out the close relationship between the blood and the joint fluid, as shown by the similarity in the contents of both fluids

*Healing in Injuries of the Carpal Scaphoid*—Johnson<sup>68</sup> carried out a series of experiments on animals to demonstrate the reparative processes after injury in the short cancellous aperiosteal type of bone, such as the carpal scaphoid. The same operative procedure was performed in each of a series of adult dogs. In one forepaw the scaphoid was fractured with an osteotome, in the scaphoid on the opposite side a deep defect was created with a small drill. At the same time, in the corresponding radius, an osteotomy was performed or a defect made in the lower third of the bone. The dogs were then killed at various time intervals up to six weeks. From a study of the specimens thus obtained the author drew the following conclusions: 1 Bone repair takes place in the scaphoid in exactly the same manner as in the medulla of the diaphyses, but the process is not as active or as extensive. 2 There is no interference with vascularity of the fragments which would cause necrosis, delayed union, or nonunion. 3 In these experiments approximation of fragments was so close that mobility or displacement did not play any part in retarding union. 4 Lytic action of the synovial fluid was not observed. 5 Lack of all periosteal callus is a large factor in causing slower union. 6 Fractured hyaline cartilage heals by fibrous tissue, and adjacent but undamaged hyaline cartilage also often undergoes fibrous change. This gives rise to permanent changes of the articulating surfaces and is probably the element most responsible for poor functional results seen clinically in these fractures. 7 All bones of this cancellous type healed more slowly than the long bones. This is due largely to the lack of subperiosteal callus formation, but it is also due, in part, to the cancellous reaction being less extensive and less active than is the medullary response in the diaphysis.

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68 Johnson, R. W., Jr. J Bone & Joint Surg 9 482 (July) 1927

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juice secreted and in the degree of acidity were found in normal persons, although repeated examinations on the same person varied but slightly. Here, again, a normal curve of secretion cannot be constructed.

#### USE OF HISTAMINE

Previous to the publication of these papers, I had decided on histamine, or one of its compounds, as a standard stimulus for secretion of gastric juice. The ability of this compound to stimulate gastric secretion was studied by Popielski,<sup>2</sup> who showed, by section of the vagi, that the drug acts directly on the gland cell. The clinical use of histamine in the study of gastric secretion was advocated by Carnot and Libert,<sup>3</sup> and has since been resorted to mostly in differentiating types of achylia. This drug was preferred because it can be procured in a stable form and is administered by hypodermic injection, so that the factor of dilution of gastric secretion by the stimulating substance is avoided. The amount of fluid withdrawn from the stomach every ten minutes represents, then, pure gastric juice, minus the amount lost during that time through the pylorus plus the amount added to the gastric contents by the regurgitation of duodenal fluid through the pylorus. This factor of regurgitation will be discussed later. The amounts gained this way, or lost by escape through the pylorus, cannot be measured accurately, and what is assumed to be the amount of gastric juice secreted is really the resultant of the three phenomena of secretion, regurgitation and loss through the pylorus.

The curve obtained after intramuscular injection of 1 mg of histamine into the normal dog is shown in chart 1. The stomach was emptied by thorough aspiration every ten minutes and 10 cc titrated with tenth-normal sodium hydroxide, using Topfer's reagent as an indicator for free hydrochloric acid and phenolphthalein as an indicator for total acidity. These results are expressed in the amount of tenth-normal sodium hydroxide necessary to neutralize 100 cc of gastric juice, because this method is the one in common use. The effect of the drug is noticed in the first aspiration made, and the highest degree of acidity is reached from thirty to forty minutes after injection. This is equivalent to 0.45 per cent of hydrochloric acid, slightly less than the degree of acidity of pure gastric juice as secreted. Variations from the foregoing curve were not marked in normal dogs, in no case being more than 10 during the first sixty minutes of the examination. The amount of secretion during a ten minute period for the first sixty minutes varied from 10 to 20 cc, occasionally more, early in the examination, while the lesser amounts were recovered toward the end. Although this method

2 Popielski, L. *Pflüger's Arch f d ges Physiol* **178** 215, 1920

3 Carnot, P., and Libert, E. *Médecine* **6** 757, 1924

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juice is a constant occurrence in the resting, as well as in the active, stomach was shown by Spencer and others,<sup>6</sup> who found trypsin in the gastric contents, the amount of the enzyme varying inversely with the degree of acidity. The common error has been to regard the presence of bile in the stomach as an index of regurgitation. Bile is not produced in response to high gastric acidity and is emptied into the duodenum in spurts of small amounts at a time, depending on the tonus of the duodenal musculature. On the other hand, the pancreatic juice is secreted in direct response to gastric acidity, and one of its functions is to neutralize the latter before the acid reaches the much more sensitive intestinal mucosa. It also finds its way into the duodenum by two openings, one entirely independent of the opening of the bile duct and

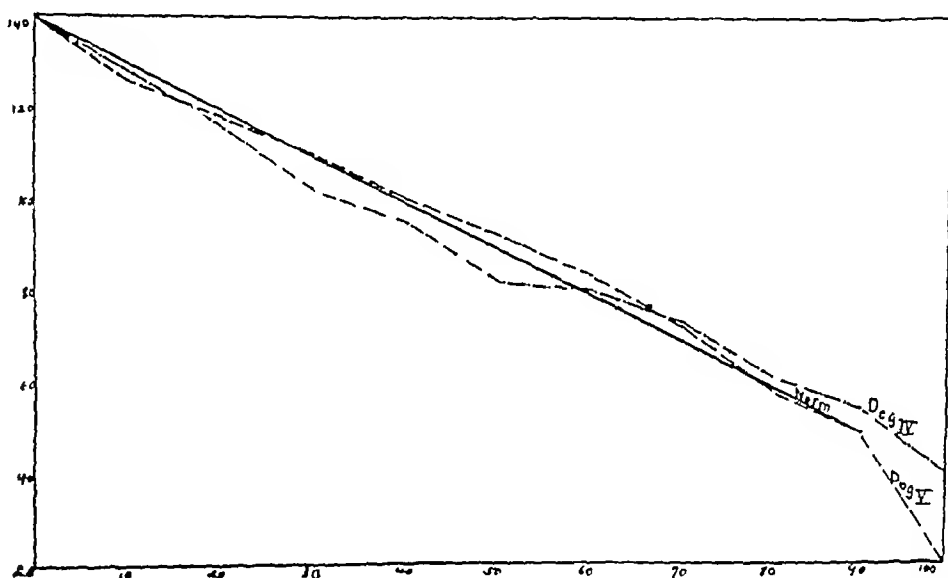


Chart 2—Curve of decrease in gastric acidity after introduction of 200 cc of 0.5 per cent hydrochloric acid into stomachs of normal dogs. The heavy black line is the average normal curve, the broken lines show the slight deviation from this norm of two dogs.

the other separated from it in a large percentage of cases. The whole mechanism, then, is one of protecting the intestinal mucosa from the acid. In regurgitation experiments made by Elman<sup>6</sup> on dogs with complete duodenal fistulas, the gastric acidity was reduced slightly, and then by intestinal juices brought to the stomach from low in the intestinal tract by antiperistalsis. The prepylorus, pylorus and first portion of the duodenum can be regarded as a single organ the function of which is that of a mixing chamber. The result of this activity is illustrated in chart 2, following the introduction of 200 cc of 0.5 per cent hydrochloric acid

<sup>6</sup> Spencer W. H., Meyer, Rehfuess M. E., and Hawk P. B. *Am. J. Physiol.* **39**: 459, 1915.

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of the extrinsic nerves on the motor activity of the stomach. There has been considerable difference in the results obtained, as may be seen by comparing the recent work of Hughson<sup>7</sup>, McCrae, McSwiney and Stopford<sup>8</sup> and Latarjet<sup>9</sup>. The latter found a marked increase in the emptying time following section of the branches of the vagi in the abdomen. McCrae and his co-workers concluded that with the exception of a temporary change shortly after the operation, the only variation in motor function which occurred was some reduction in the initial emptying time. Hughson, using a simpler opaque mixture introduced directly into the stomach, found a constant definite decrease in the emptying time; he also found that following section of the vagi or its branches, reflex spasm of the pylorus could not be produced later, a phenomenon which can always be brought about in an animal with intact vagi. In other words, in these animals there resulted a hypotonus of the pylorus which allowed increased patency of the pyloric lumen.

Section of the branches of the nerve entering the stomach has been reported clinically by Wertheimer and Latarjet,<sup>10</sup> who performed this procedure on twelve patients; they sometimes combined it with some other operation on the stomach. In these cases, the preoperative conditions and function of the stomach are not always clear, and the postoperative examinations as reported are not conclusive. None of these patients had peptic ulcers. Schiassi<sup>11</sup> advocates this method of treatment for patients with gastric and duodenal ulcer, either alone or accompanied by one of the operations usually performed; he does not offer any clinical or experimental evidence, however, on which to base his procedure.

The experiments described were carried out by me during the course of an investigation of the physiologic end-results after operative treatment for peptic ulcer. They were carried out on dogs which were first subjected to the two methods of examination already described. Then the nerves supplying the stomach were sectioned in one of three following ways: 1. Section was made intrathoracically, because by this method any change due to peritoneal irritation was avoided and because the vagus branches only were sectioned. 2. The branches were sectioned in the abdomen, the two large trunks being severed as they came through the diaphragm, one on the anterior and the other on the posterior surface. The smaller branches were cut to make certain of

7 Hughson, W. Effect of Vagus Neurotomy on Pyloric Sphincter, *J. A. M. A.* **88** 1072 (April 2) 1927.

8 McCrae, E. D., McSwiney, B. A., and Stopford, J. S. B. *Quart. J. Exper. Physiol.* **16** 195, 1926, *ibid.* **15** 201, 1925.

9 Latarjet, A. *Bull. Acad. de med., Paris* **87** 861, 1922.

10 Wertheimer, P., and Latarjet, A. *Presse méd.* **31** 993, 1923.

11 Schiassi, B. *Ann. Surg.* **81** 939, 1925.

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Chart 3—Curve of secretion after injection of histamine, following section of vagi intrathoracically

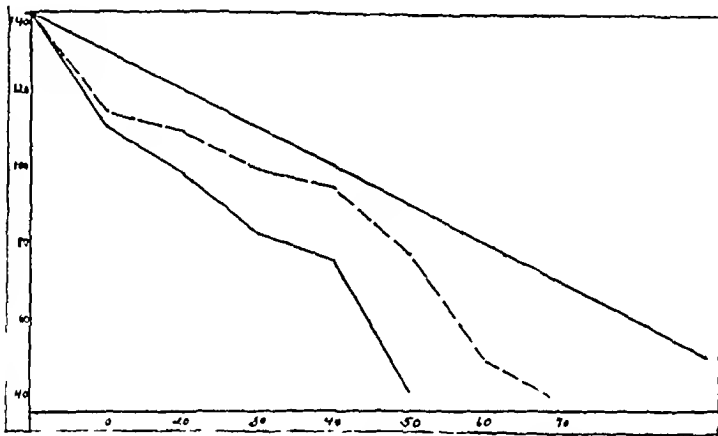


Chart 4—Neutralization of gastric contents after introduction of 0.5 per cent hydrochloric acid. Results obtained in two cases following section of the vagi intrathoracically as compared with the average normal curve, which is represented by the heavy black line

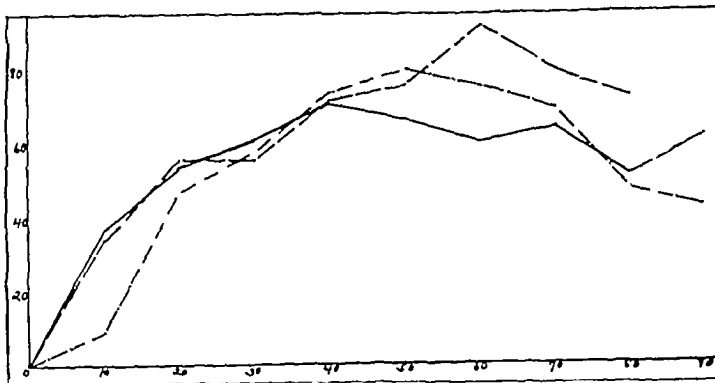


Chart 5—Curve of secretion of hydrochloric acid after injection of histamine obtained in three dogs after section of the vagi intraperitoneally

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## PYLOROPLASTY

The Finney pyloroplasty was performed on another series of dogs. The curves obtained from one of these animals are seen in charts 9 and 10. All the animals reacted in a manner similar to that of the one used as an illustration. After the administration of histamine, the hydrochloric acid secreted in the gastric juice does not reach 90 (0.32 per cent). The reason for this is probably the same as that mentioned, the regurgitation of alkaline pancreatic juice to neutralize the acid as it is secreted. This regurgitation is most marked after the introduction of 200 cc of 0.5 per cent hydrochloric acid into the stomach. Chart 10 shows the curve obtained one month after operation. There is a uniform sharp decrease in acidity, with shortening of the emptying time to fifty and sixty minutes. A large stoma with no control of the sphincter replaces the natural opening. As the acid comes in contact with the duodenal mucosa, the pancreatic juice is secreted and immediately enters the stomach, where the acid is neutralized. With this large opening and free access between the duodenum and the stomach, this neutralization takes place more quickly, and the plotted curve is much more distant from the norm than is the case with any of the other procedures. As the optimum reaction is reached sooner, the stomach empties in much less time.

## COMMENT

In the many different methods of gastric analysis, the phenomenon of regurgitation is not considered. A reading of titratable acidity or alkalinity in the stomach at any given time is the mean of two opposing forces, secretion of gastric juice and its neutralization by regurgitant duodenal fluid, which owes most of its effectiveness to the highly alkaline pancreatic juice. The regurgitation of the latter fluid into the stomach is a constant occurrence in the resting as well as in the digesting stomach, a fact which has been corroborated in many ways. The duodenum, pylorus and prepylorus might well be considered a single organ, for they have one important function in common, that of a mixing chamber in which the chemical reaction of their contents is adjusted to the optimum which can be tolerated by the intestines. This phenomenon, then, is of the utmost importance in the process of digestion, and a test of the stomach's function resolves itself into a test of this function of neutralization. To measure this accurately, a direct application of the phenomenon described by Boldyreff is advocated, *i. e.*, the introduction of 200 cc of 0.5 per cent hydrochloric acid into the stomach, with examination of the contents every ten minutes. From observations made during the examination of many dogs by this method, a normal curve is constructed, from which there are minor individual deviations. Following the various operative procedures, the curves





of histamine is preferable, because the psychic phase of secretion is avoided by subcutaneous administration, a standard amount of a known substance is given, the factor of dilution is avoided, and one is nearer to recovering pure gastric juice, the only dilution being the regurgitated duodenal fluid

The results reported are those obtained on dogs, the results of clinical application will be reported at a later date

#### CONCLUSIONS

1 Regurgitation of duodenal fluid into the stomach is a constant occurrence The important constituent of this fluid is the pancreatic juice

2 Neutralization of gastric acidity by this regurgitating fluid is an important part of digestion

3 This rate of neutralization can be measured accurately, and can be made a part of every gastro-intestinal examination

4 Rapid decrease in acidity is the ideal result following operation for ulcer of the stomach This is brought about by the large stoma resulting either from resection or from pyloroplasty If the stoma is small when ordinary gastro-enterostomy is performed, the necessary amount of regurgitation does not occur

5 Intrathoracic or intraperitoneal vagotomy results in decreased tonicity of the pylorus This is reflected in the more rapid emptying and the decrease of gastric acidity



ephedrine by mouth and to epinephrine subcutaneously. There was recurrent urticaria for several days. Mild desquamation occurred, most extensively at the site of cellulitis, from March 10 for about four days. The area of cellulitis was marked for a time by a brownish tint, but returned to normal. The toe healed completely, and the patient was discharged, well, on March 17, 1927.

Bacteriologic study was conducted as follows: saline was injected at the edge of the area of cellulitis on February 25 (the day after admission) and on February 26. It was withdrawn and cultured, but a growth was not obtained. On February 25, a throat culture showed approximately 5 per cent of hemolytic streptococci, several strains of which were isolated. Pure cultures of hemolytic streptococci were found in pus from the abrasion on the toe on February 26 and 27. The organisms from the toe and throat cultures were studied further, they proved to be short chained, gram-positive cocci, producing typical beta hemolysis in poured blood-agar plates. They did not ferment mannitol in ascitic fluid broth. Growth in broth was flocculent, but emulsion made from ascitic fluid agar slopes proved to be stable and were used for agglutination. Several strains of the throat and toe cultures agglutinated to the titer of a scarlatinal streptococcus antiserum prepared with Dick strain 25<sup>6</sup>. Flasks of Douglas broth were inoculated and in two to four days, the growth was passed through Berkefeld V filters, 0.5 per cent phenol was added and dilutions made for skin testing. Both the throat and toe strain filtrates in a dilution of 1:100 caused a sharp localized erythema when injected intracutaneously in doses of 0.1 cc in persons with a positive Dick reaction. We repeatedly obtained inhibition of erythema with the organism cultured from the toe, when the filtrate dose was mixed with 1 unit of scarlet fever antitoxin (Dochez type). Proper controls, with due account for dilution, were made in each case. The filtrate from strains isolated from the throat, however, produced an erythema not influenced by previous admixture with scarlet fever antitoxin, even when the unit erythema dose of filtrate (0.1 cc of 1:100 dilution) was combined with as high as 20 units of antitoxin. This observation was checked several times with different lots of antitoxin.

We feel that this definitely classifies the organism from the initial lesion on the toe as *Streptococcus scarlatinae*. By culture, agglutination and neutralization of the skin toxin which it produced, it fulfilled all criteria. We did not feel justified in attempting to reproduce the disease in man. The streptococcus isolated from the throat, however, failed to qualify either clinically, in view of the absence of angina, or serologically, in that the toxin which it produced was not neutralized by scarlet fever antitoxin. The production of a skin toxin not neutralized by standard scarlet fever antitoxin has been observed by Kirkbride and Wheeler<sup>7</sup> with streptococci from scarlet fever and from other sources also. Hence we consider that this patient had scarlet fever. The causative organism

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6 We are indebted to Dr. S. Bayne-Jones of the Department of Bacteriology for this agglutinating serum.

7 Kirkbride, Mary B., and Wheeler, Mary W. Studies of the Toxins of the Hemolytic Streptococci Associated with Scarlet Fever, *J. Immunol.* **11**: 477 (June) 1926, Further Observations on the Toxins of Hemolytic Streptococci, *J. Immunol.* **13**: 19 (Jan.) 1927.



# COLLAPSE FOLLOWING SUDDEN DECOMPRESSION OF THE DISTENDED ABDOMEN

A STUDY IN EXPERIMENTAL ASCITES \*

OWEN H WANGENSTEEN, M D

AND

HORACE G SCOTT, B A

MINNEAPOLIS

In tapping the abdomen of the patient with marked ascites, the necessity for caution in removing the fluid slowly is well known. To obviate the collapse of the patient consequent on the too rapid removal of the transudate, a Scultetus bandage or a binder is frequently placed around the abdomen at the start and is tightened as the fluid is removed. The same prudence in performing paracentesis of the pleural cavity is a matter of every-day practice. On consulting a large number of modern surgical texts, we have been unable to find a word of caution in this regard in the matter of incising the distended abdomen. In discussing the subject with several of our preceptors and colleagues, however, we find that most of them know of or have had personal experience with instances in which collapse followed directly on the sudden decompression of the distended abdomen by incision. The synopses of the records of two patients in whom this phenomenon occurred and who were observed in the surgical service at the University Hospital follow.

## REPORT OF CASES

CASE 1—A boy, aged 15, was admitted to the University Hospital, May 22, 1925, and was discharged, June 14, 1925.

About 5 p. m., on May 21, the patient was kicked in the lower left abdominal quadrant by a horse. He was knocked down and lay in a faint for about three minutes. When picked up by his mother, he complained of severe pain over the entire lower part of the abdomen.

At 3 p. m., on May 22, he was brought to the University Hospital. At this time he complained of pain on respiration above the left clavicle.

On examination, the boy was found to be well developed and well nourished. There was a slight cyanosis of the mucous membranes of the lips. He did not appear to be in great distress, but complained that movement caused him pain. The pulse was full and strong, the rate being about 90 beats a minute, the temperature was 98.8 and the respirations, 22, the systolic blood pressure was 124, diastolic, 82. Results of the examination of the chest were negative. The abdomen was moderately distended and exhibited "choc en retour." On palpation it was found uniformly tender. Dulness on percussion was demonstrated in the flanks. The midportion of the abdomen was tympanitic. Movable tympani could not be demonstrated. On auscultation of the abdomen, peristaltic movements were not heard. Rectal examination showed that bulging was present and that the region was moderately tender.

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\* From the Department of Surgery of the University of Minnesota.



# COLLAPSE FOLLOWING SUDDEN DECOMPRESSION OF THE DISTENDED ABDOMEN

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In tapping the abdomen of the patient with marked ascites, the necessity for caution in removing the fluid slowly is well known. To obviate the collapse of the patient consequent on the too rapid removal of the transudate, a Scultetus bandage or a binder is frequently placed around the abdomen at the start and is tightened as the fluid is removed. The same prudence in performing paracentesis of the pleural cavity is a matter of every-day practice. On consulting a large number of modern surgical texts, we have been unable to find a word of caution in this regard in the matter of incising the distended abdomen. In discussing the subject with several of our preceptors and colleagues, however, we find that most of them know of or have had personal experience with instances in which collapse followed directly on the sudden decompression of the distended abdomen by incision. The synopses of the records of two patients in whom this phenomenon occurred and who were observed in the surgical service at the University Hospital follow.

## REPORT OF CASES

CASE 1—A boy, aged 15, was admitted to the University Hospital, May 22, 1925, and was discharged, June 14, 1925.

About 5 p m, on May 21, the patient was kicked in the lower left abdominal quadrant by a horse. He was knocked down and lay in a faint for about three minutes. When picked up by his mother, he complained of severe pain over the entire lower part of the abdomen.

At 3 p m, on May 22, he was brought to the University Hospital. At this time he complained of pain on respiration above the left clavicle.

On examination, the boy was found to be well developed and well nourished. There was a slight cyanosis of the mucous membranes of the lips. He did not appear to be in great distress, but complained that movement caused him pain. The pulse was full and strong, the rate being about 90 beats a minute, the temperature was 98.8 and the respirations, 22, the systolic blood pressure was 124, diastolic, 82. Results of the examination of the chest were negative. The abdomen was moderately distended and exhibited "choc en retour." On palpation it was found uniformly tender. Dulness on percussion was demonstrated in the flanks. The midportion of the abdomen was tympanitic. Movable tympani could not be demonstrated. On auscultation of the abdomen, peristaltic movements were not heard. Rectal examination showed that bulging was present and that the region was moderately tender.

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\* From the Department of Surgery of the University of Minnesota.





explanation of which is to be found in compression of the inferior vena cava with a diminished return of blood to the right side of the heart. He<sup>4</sup> also believed that excessive intra-abdominal pressures caused death by heart failure rather than by interfering with respiration. Thorington and Schmidt<sup>9</sup> (1923) too recorded the effects of an increase on blood pressure. They found that the changes in the general circulation were not constant, but usually a fall of from 5 to 10 mm of hemoglobin was observed in the arterial pressure when the ascites established inhibited the excretion of urine. Often after an initial fall the blood pressure was observed to rise to a point higher than it was originally when the intra-abdominal pressure was maintained at a pressure of 30 mm of hemoglobin (40.5 cm of water). Coombs<sup>6</sup> stated that an appreciable rise in carotid pressure was never obtained following the gradual introduction of fluid into the abdominal cavity, but in several instances, the removal of the fluid was accompanied by a distinct rise in arterial pressure.

We have failed, however, to find any reference to a study or investigation relative to the sudden release of increased intra-abdominal pressure on the arterial pressure. Believing that the collapse that occasionally follows the sudden decompression of a distended abdomen might be duplicated and elucidated in such an experiment, we have put it to experimental test. In this study of experimental ascites we have concerned ourselves with this issue only.

#### METHOD

An increased intra-abdominal pressure was established in twelve dogs by inserting a glass cannula with a flange into the peritoneal cavity and closing the abdominal wall tightly about it. Water was run into the peritoneal cavity by gravity. In order to establish excessive pressures, a hand pump was attached to the large gravity bottle, and air was pumped in above the fluid. The pressure in the abdomen was recorded by a Y connection to a mercury manometer. The arterial pressure was obtained from the carotid artery. Both arterial and intra-abdominal pressures were recorded on a revolving drum. No measurements of the normal intra-abdominal pressure were made. The intra-abdominal pressures used were higher than those observed in most patients with ascites. A constantly uniform intra-abdominal pressure could not be maintained, owing to the gradual stretching of the abdominal wall. The effect of sudden decompression of the abdomen by quick incision was noted. All experiments were performed under ether anesthesia.

#### COMMENT

Experimental ascites was established in twelve dogs, water pressures averaging from 40 to 50 cm of water being employed. In a few animals this pressure was exceeded at times, and again lower pressures were

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<sup>9</sup> Thorington, J. M., and Schmidt, C. F. A Study of Urinary Output and Blood Pressure Changes Resulting from Experimental Ascites, *Am J M Sc* **165** 880, 1923.



gradually returned to the normal level. In another dog in which the intra-abdominal pressure was increased to only 30 cm of water pressure (22 mm of mercury), only a slight and transient fall of arterial pressure accompanied the quick release of the increased intra-abdominal pressure.

The sudden decompression of the distended abdomen was also practiced in three dogs in which simple severed gut obstructions had been established in the duodenum two days previously. In these animals, the dyspnea caused by the same increase in intra-abdominal pressure was considerably more in evidence. In experiment II in the accompanying illustration is shown the fall in blood pressure in such an animal caused by the increase in intra-abdominal pressure. Following the sudden release of the ascites by incision, death occurred in two of the three animals. In the other animal, a marked reduction of arterial pressure was observed, but the blood pressure was gradually reestablished at the normal level as obtained following quick release of the increased pressure in the normal animal.

In the five other dogs for which tracings were made, an attempt was made to determine what factors would diminish or inhibit this fall in arterial pressure. In experiment III, the slight reduction accompanying gradual decompression of the distended abdomen is shown. Following a sudden release of the increased intra-abdominal pressure, the usual marked fall in arterial pressure was observed. When the intra-abdominal pressure was quickly reestablished after sudden decompression, the arterial pressure also quickly rose again. In two animals it was observed that a preliminary subcutaneous administration of solution of pituitary in great measure inhibited the marked fall in arterial pressure which would otherwise follow when the distended abdomen was incised (experiment IV). In two other dogs, results of the same nature but less marked than those following the use of solution of pituitary were observed when the blood volume was increased just before or after decompression of the abdomen by transfusing 400 cc of saline solution into the jugular vein. That the increased intra-abdominal pressure probably does not completely compress the inferior vena cava is shown in experiment V. Here the experimental ascites caused an increase in the arterial pressure. Following a gradual release of the increased intra-abdominal pressure, a marked fall was obtained when the circulating blood volume was reduced by clamping the inferior vena cava.

#### SUMMARY

When the markedly distended abdomen is incised, the same precaution of decompressing it slowly, as in paracentesis of the abdomen or chest, should be observed. In practice, circulatory collapse following incision of such an abdomen apparently does not occur with any degree



at 10 45 At 10 50 the blood pressure had fallen to 138 mm, and the dog was manifesting marked evidence of dyspnea At 11 00, a blood pressure of 80 mm was present, at 11 10, a blood pressure of 60 mm Blood pressure was sustained at this level to 11 20 When the ascites was released by a quick stab of the abdomen, the pressure suddenly fell to 50 mm of mercury, and in a few minutes the dog was dead

EXPERIMENT 3 (April 27, 1927) —Experimental ascites in normal dog to illustrate the effect from the gradual and sudden release of intra-abdominal pressure The tracing was started at 4 10 The blood pressure was 150 mm The pressure was sustained at this level, and at 4 25 a cannula was introduced into the abdomen At 4 30, a water pressure of 40 cm (30 mm of mercury) was started The arterial pressure maintained itself at the same level At 4 40, the pressure was slowly released by lowering the bottle of water used to obtain the pressure No effect on the blood pressure was noted A gradual reduction of pressure to 130 mm had obtained at 4 45 At this time, the ascites was again quickly reestablished, the arterial pressure quickly rose and maintained itself at 160 mm At 4 50, the ascites was quickly released by a stab wound of the abdomen, and the arterial pressure fell to 80 mm At 4 55, the blood pressure was 100 mm of mercury Ascites was again established, and the arterial pressure gradually rose to 130 mm at 5 00 At 5 05, the pressure was still the same The ascites again was quickly released, and the blood pressure fell to 80 mm and sustained itself at this level when the experiment was discontinued at 5 15

EXPERIMENT 4 (May 6, 1927) —Experimental ascites to note the effect of solution of pituitary on the quick release of intra-abdominal pressure At 10 00, the experiment was begun The arterial pressure was 220 mm of mercury At 10 10, there was a gradual reduction to 200 mm At 10 15, the pressure was 220 At 10 20, a cannula was introduced into the abdominal wall At 10 25, arterial pressure was the same Two ampules each containing 1 cc of surgical solution of pituitary were injected at this time Pressure sustained itself at the same level At 10 30, ascites was begun At 10 40, the ascites was quickly released by a stab wound in the abdomen A sudden fall of arterial pressure to 160 mm, with recovery in two minutes to 180 mm Pressure was sustained at this level until the experiment was discontinued at 10 50

EXPERIMENT 5 (May 17, 1927) —Experimental ascites The effect of a previous intravenous injection of saline solution was noted, also clamping of the inferior vena cava The experiment was started at 10 50 The blood pressure was 180 mm of mercury A cannula was inserted into the abdomen at 11 00 The blood pressure was 160 mm At 11 10, it was the same At 11 15, experimental ascites was started, water pressure of 60 cm (45 mm of mercury) was employed Following the increase of abdominal pressure, there was a gradual fall of arterial pressure in two minutes of 120 mm of mercury with a gradual rise in five minutes to 140 mm The pressure sustained itself at this level At 11 30, 400 cc of saline solution was introduced into the right jugular vein The blood pressure rose to 160 mm of mercury and sustained itself at this level for about five minutes, then gradually fell to 140 mm at 11 50 and sustained itself at this level for about ten minutes The abdomen had meanwhile been incised with just a transient fall in pressure. At 12 00, the inferior vena cava was clamped, with a sudden fall in blood pressure to 76 mm Pressure was sustained at this level At 12 05, 400 cc. of saline solution was again introduced into the jugular vein, this caused a gradual rise in arterial pressure to 120 mm at 12 15 The clamp on the inferior vena cava was removed The blood pressure rose to 140 mm and sustained itself at this level



flexion The author felt that this method is preferable to the so-called "shelf operation"

[ED COMMENT—The figure of 60 per cent for good functional results, reported by Willard, conforms more or less closely to the figures obtained in previous studies of the end-results of the same type The bilateral dislocations present the greatest difficulties and are the ones which yield the worst results Sufficient evidence to this effect has accumulated, and we believe that we must look to open reduction in properly selected cases for further improvement in the results The value of Eikenbary's procedure cannot be judged from the report of the result in a single case]

*Congenital Clubfoot*—Orthopedic surgeons have not generally agreed as to the best method of treating patients with congenital clubfoot, some have employed forcible correction, while others have used gentle and repeated manipulation By experiments on feet that were about to be amputated, Buerkle de la Camp<sup>3</sup> tried to show that forcible methods are harmful and may cause lasting injury Dissection of the amputated specimens showed that tearing of the capsule of the joint, avulsion of cartilage and bone and, likewise, compression of the cartilage and bone had taken place The author therefore concluded that the better method is the one aiming at repeated partial corrections with absence of force He did not consider open operation necessary in children

*Hereditary Hypermobility of Joints*—Key<sup>4</sup> reported the study of a "double-jointed" family, in which the abnormal hypermobility of the joints is present in all of the male members, and is absent in all of the females The condition appeared in the father and was not present in his parents, in any of his nine brothers or in his sister It was transmitted by the father to all of his four sons, but not to any of his daughters It thus acts as a "sex linked characteristic"

#### DISTURBANCES IN THE GROWTH OF BONE

*Coxa Valga and Osteochondritis*—Ettorre<sup>5</sup> discussed the theories regarding the causes of coxa valga, especially the one expressed in an article by Walter Mueller, who considered that the cause of coxa valga is an outward displacement of the epiphysis of the head on the neck From a study of roentgenograms in his own cases, Ettorre drew the

3 Buerkle de la Camp, H München med Wchnschr **74** 974 (June 10) 1927

4 Key, J Albert Diagnostic Problems in Hip in Early Life, J A M A **88** 1710 (May 28) 1927

5 Ettorre, E Policlinico **34** 58 (Feb 15) 1927





Recent studies seem to show that the substance present in ordinary sterols of both animal and plant origin, which is responsible for their activation by ultraviolet rays into antirachitic potency, is ergosterol or some kindred substance. Rosenheim and Webster<sup>8</sup> made tests of irradiated ergosterol which showed an astonishing degree of potency. A daily dose of 0.0001 mg. cured and prevented rickets in rats kept on a rachitogenic diet. Even this does not represent the maximal antirachitic potency of the new product. The authors stated that 5 mg. is equivalent to 1 liter of a good cod liver oil. At the same time a dose 10,000 times greater than what is now regarded as an effective dose did not produce any obvious ill effects on rats. The authors concluded that the naturally occurring parent substance of vitamin D is ergosterol or a sterol possessing the same absorption spectrum and physiologic activity.

Kramer and his associates<sup>9</sup> succeeded in preparing a cholesterol-free concentrate of cod liver oil which has the same antirachitic potency as cod liver oil. When injected subcutaneously in an ether solution the concentrate cured experimental rickets in rats. The same concentrate was inactive when injected subcutaneously with palmitin as the solvent.

Smith<sup>10</sup> made a study of the incidence of rickets in 597 children living under excellent hygienic surroundings in a small city in the western Rocky Mountain region, with the same latitude as New York City and an elevation of 4,310 feet. Of these children, 18.2 per cent were found to have rickets. The author felt that this low incidence is to be accounted for by the good hygienic conditions, the abundant sunshine and outdoor life and the greater values in ultraviolet radiations of the sunlight at this altitude.

*Osteomalacia*—Chabrol and his associates<sup>11</sup> reported the observations at necropsy in a well known case of osteomalacia, that of a man (Godezeme) who had provided the material for numerous reports by Berger from 1899 to 1905. After twenty-five years passed in a Bonnet's apparatus, the man died from pneumonia, in 1922. The case is of interest, first, because it occurred in a man, and Durham was able to find only 13 such cases out of 145 reported in the literature and, second, because the disease had undergone a spontaneous resolution, whereas usually it progresses rapidly in men, with death at the end of from four to five years, the extreme limits being one and eleven years. The osteo-

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8 Editorial, J. A. M. A. **88** 1969 (June 18) 1927

9 Kramer, B., Kramer, S. D., Schelling, D. H., and Shear, M. J. J. Biol. Chem. **71** 699 (Feb.) 1927

10 Smith, E. H. California and West Med. **26** 341 (March) 1927

11 Chabrol, E. Presse med. **35** 275 (March 2) 1927

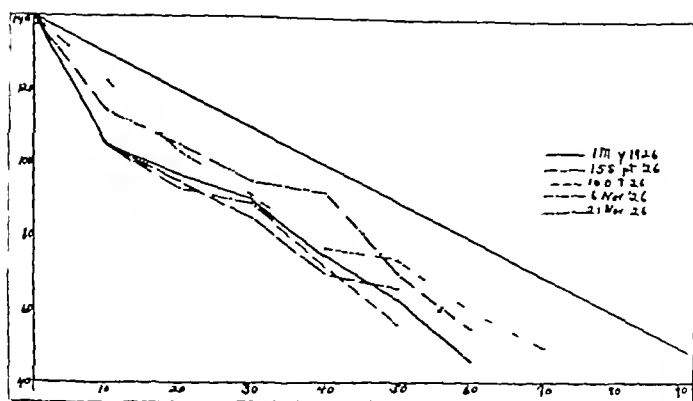


Chart 6—Neutralization of gastric acidity after administration of 0.5 per cent hydrochloric acid. Results obtained in a dog treated by intraperitoneal section of the vagi over a period of seven months following operation and compared with the average normal curve which is represented by the heavy straight line.

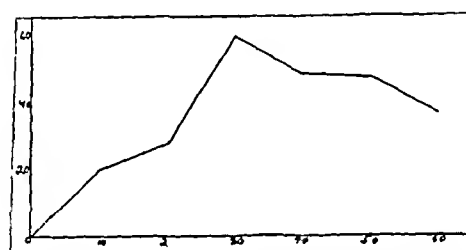


Chart 7—Secretion of hydrochloric acid after injection of histamine in a dog in which the intrinsic nerve supply of the stomach was sectioned by incision of the muscularis and submucosa.

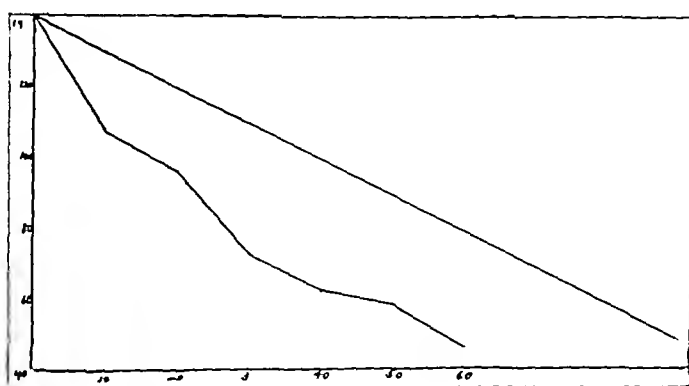


Chart 8—Neutralization of gastric acidity after administration of 0.5 per cent hydrochloric acid in a dog treated with circumcision of the gastric muscularis and submucosa and compared with the average normal curve which is represented by the heavy straight line.

resected specimens On careful examination, Koenig found them present in more than 50 per cent He was able to demonstrate them roentgenologically, however, in only twelve of ninety-eight cases From comparison of the roentgenograms with the specimens, he concluded that a cavity in the bone filled with tuberculous granulations can usually be shown, but that minute foci and infarcts cannot be seen

[ED COMMENT—This article serves only to emphasize what has been frequently pointed out before, namely, that absence of involvement of the bones cannot be claimed except after repeated and prolonged search of the specimen The more carefully the material is studied microscopically, the more constantly foci are found in the bone ]

*The Significance of Abscess in Pott's Disease*—Massart and Ducroquet<sup>14</sup> were convinced that abscess is a constant part of the lesion of vertebral tuberculosis and not merely a complication of it It is of the greatest possible diagnostic significance, and in cases in which the diagnosis is in doubt the roentgenologic examination should be repeated until one is certain of either the absence or the presence of abscess In the lumbar and cervical regions, the abscess is of the migrating type and can usually be palpated In the dorsal region, the abscess is confined by the vertebral ligaments and remains concealed except for roentgenologic demonstration

*Catheterization of Spinal Abscess*—In describing his technic for relieving the pressure of the abscess on the spinal cord in patients with Pott's disease with paraplegia, Calvé,<sup>15</sup> stated that a canaliculated sound, appropriately curved, is introduced into the anterior extradural space through the intervertebral foramen, effecting a kind of catheterization Pus appears in the sound immediately after puncture, aspiration usually being unnecessary He employed this procedure sixty-six times, and it has never led to any ill effects except in one instance in which it occasioned girdle pains He treated eighteen patients with grave paraplegia by this method, and ten of them remained under observation long enough for him to know the results In seven the paraplegia disappeared, although previous orthopedic treatment, which had been continued for months, had not been of any avail

[ED NOTE—One of the editors saw several of the patients who were treated by Calvé and has been impressed with the method which on demonstration seems safer and easier than would appear from the description ]

14 Massart, R, and Ducroquet, R Arch franco-belges de chir 29 181 (March) 1926

15 Calvé, Jacques Arch franco-belges de chir 29 218 (March) 1926



when the line of demarcation between dead and living bone has become well defined, and when enough new bone has formed to insure the strength of the shaft Thornton described his operation procedure as a "sculpturing operation," in which the diseased area was thoroughly exposed with the aid of a tourniquet, all bone sinuses were eliminated, and all bone cavities made shallow Incisions should be made whenever possible so that muscle flaps will be made available to fill in the cavities The wound is packed with dry gauze, which is removed in five days, and thereafter daily dressings are made with gauze coated with petrolatum

#### ANTERIOR POLIOMYELITIS

*Experimental Poliomyelitis in Rabbits*—Jemma<sup>19</sup> made a careful experimental study of poliomyelitis in rabbits and drew the following conclusions 1 It is possible to reproduce anterior poliomyelitis experimentally in rabbits by injections of cerebrospinal fluid from sick children provided that young animals weighing not more than 700 or 800 Gm are chosen and that the cerebrospinal fluid used is from children who have been ill for from one to five days 2 Transmission is possible from rabbit to rabbit, an emulsion of infected nerve substance either direct or preserved in glycerine for several months being used

[ED COMMENT—We believe that heretofore it has usually been considered impossible to reproduce experimental poliomyelitis in any other animal than the ape ]

*Results of Treatment with Poliomyelitis Antistreptococcus Serum*—Rosenow and Nickel<sup>20</sup> summarized their results in the treatment of acute poliomyelitis with poliomyelitis antistreptococcus serum as follows

Altogether, the results in 1,113 patients with poliomyelitis who received serum and in 278 control untreated patients are illuminating The mortality rate was found to be much lower in the treated than in the control group, especially when the serum treatment was begun early, even if there were bulbar symptoms This was true in each of the four age groups (up to five years, from 6 to 10, 11 to 15, 16 years or more) in each of the five years from 1921 to 1925 as well as in each epidemic studied

The incidence of residual paralysis was also much lower in the treated than in the control group, especially in those patients who received serum before or soon after slight paralysis had developed The mortality rate and the incidence of residual paralysis in the control group were not abnormally high and correspond closely to those untreated patients whose cases are reported in the literature The incidence of the more severe initial symptoms, the average cell count, and the incidence of initial bulbar types of disease were somewhat higher in the treated than in the control group The age incidence was about the same in the two groups The good effect of the serum occurred inde-

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19 Jemma, G *Pediatrics* **34** 1363 (Dec 15) 1926

20 Rosenow, E C, and Nickel, A C Treatment of Acute Poliomyelitis with Poliomyelitis Antistreptococcus Serum, *Am J Dis Child* **33** 27 (Jan) 1927



*Metabolism in Rheumatism*—Ellis<sup>22</sup> believed that all forms of rheumatism are fundamentally biochemical in origin and that the variety is largely determined by the constitutional characteristics of the person affected. He believed that these characteristics can be definitely recognized and classified by an examination of the urinary secretions. Life as biochemically considered is chiefly an acid function in an alkaline or neutral medium. The fires of life are producers of acid. The metabolic balance of an organism will depend on its capacity for producing acid, and the balance can be ascertained by a study of the acid excreted in the urine. This excretion is in two forms—free acid and acid combined with ammonia. An acid constitution is that in which the free acid is approximately the same as the combined acid. When the ratio is two to one in favor of the ammonia combined acid, one has the average normal or balanced constitution, and in the third group, which is relatively deficient in free acid, a proportion of three or more to one, one has the alkaline constitution. Ellis said that rheumatism is a metabolic condition and can be divided into four essential metabolic groups:

- 1 Arthritis deformans or progressive polyarthritis, the so-called septic variety. This is caused by general metabolic deficiency, presents the characteristics of a trophic neurosis, and results principally from a deficiency in phosphoric acid but is frequently activated by aseptic forms.
- 2 Osteo-arthritis, which results from a general metabolic excess without essential neurotic involvement. It is caused by accumulation of waste material through deficient elimination. It is principally activated by trauma or overwork of the part involved.
- 3 Climacteric arthritis due to want of glandular balance, which is described as endocrine arthritis. It is caused by functional changes similar to those produced by the menopause, and it is sometimes activated by a septic focus.
- 4 Gouty arthritis, which is due to uric acid and is produced by excess deposits of sodium urate and deficient elimination of uric acid resulting from derangement of the purin metabolism. The treatment of patients with metabolic deficiency has been directed to remedying the deficiency in assimilation and giving acid tonics and metabolic stimulants. This is largely a disease caused by deficiency in phosphoric acid. The type of rheumatism caused by metabolic excess requires the opposite type of treatment, as the deposits are the result of metabolic combustion in excess of the eliminating capacity. Fluids are demanded in this form, with the exception of partially fermented alcohol or sugary drinks.

*Dysenteric Arthritis*—According to Besson and Ehringer,<sup>23</sup> the agglutination reaction is of aid in the diagnosis of dysenteric arthritis. They reported a case in which the knee and elbow joints became inflamed.

22 Ellis, H. A. M. J. & Record **125** 437 (April 6) 1927.

23 Besson, A., and Ehringer, G. Paris med **2** 329 (Oct 30) 1926.





## DISTURBANCES OF THE NERVES

*Cortical Injections for Athetosis*—Although it is still a matter for discussion whether athetosis is due to disturbances of the cortical or subcortical centers, Nasaroff<sup>33</sup> reported that he has been able to obtain striking results in typical cases by the injection of alcohol in the cortex of the affected area, according to the method of Rasumowsky. He considered this method less dangerous than Horsley's operation. He described a case in which the involuntary motions of the hand ceased a few weeks after the injection, voluntary motions returned, and the hand again became useful. In another case, 0.5 cc of 80 per cent alcohol was injected into the region of the arm and hand centers. For the first few days after operation the hand was parietic, and soon afterward active motions were noted. Two months later, the patient was able to use the hand for definite tasks, and the athetoid movements had not reappeared.

## CIRCULATORY DISTURBANCES

*Trophic Disturbances in Buerger's Disease*—Boyer and Thibault<sup>34</sup> called attention to the possibility of Buerger's thrombo-angitis obliterans being due primarily to neurotrophic disturbance. Analysis of the case histories showed that pain was the first symptom, and they believed that this pointed to a neuritis. They also found evidences of trophic disturbances, and they believed that there are cerebrospinal symptoms antedating the appearance of the vascular lesions. As long as the origin of the condition is unknown, one should be on the lookout for evidences of disturbance of the nerves, and in cases coming to autopsy the examination should include systematic search for minute lesions in the cerebrospinal and sympathetic systems. Boyer and Thibault suggested a neurotrophic virus as the real etiologic factor.

*Innervation of Vessels*—Magnus<sup>35</sup> made a study of the innervation of blood vessels and used the capillary microscope and photographs to record the changing conditions. He was unable to find any physiologic, or even a theoretical basis, for the operation of periarterial sympathectomy. Local rises in temperature and hyperemia are noted after many operations and traumatic disturbances, and it is only in this way that he can account for the reputed benefits of the operation.

*Histologic Changes in the Vessel Walls After Sympathectomy*—Jegorov<sup>36</sup> performed experimental periarterial sympathectomy in twenty-six dogs and obtained specimens of the vessels operated on at different periods, in order to follow the changes consequent to the opera-

33 Nasaroff, N. N. *Zentralbl f Chir* **54** 1478 (June 11) 1927.

34 Boyer, G., and Thibault, G. *Presse med* **35** 100 (Jan 22) 1927.

35 Magnus, G. *Arch f klin Chir* **143** 574, 1926.

36 Jegorov, B. *Russkaja klinika* **2** 46, 1924.



paring these with the failures, the author stated that there were nineteen deaths, two of them being due to suprarenal deficiency, and that in addition there were a number of postoperative accidents. Herzberg concluded that the operation has been based purely on hypothetical grounds, and that lacking anatomicopathologic and biochemical foundations, it has also failed to receive any justification from the clinical side.

[ED COMMENT—We believe that this sweeping denunciation of the operation of suprarenalectomy which is based on the author's personal experience and on careful investigation of the experience of others ought to settle the place of the operation in the treatment of circulatory disturbances.]

to be negative. Wagoner<sup>5</sup> (1926) recently also recorded subatmospheric measurements of intra-abdominal pressure on patients, animals and cadavers.

Emerson carried out experiments on rabbits, cats, dogs and calves. A slightly positive intra-abdominal pressure was usually observed. Debilitated states were found to show low pressures. With ether anesthesia and a complete loss of muscular tone, readings reaching zero or atmospheric pressure were observed. In quiet respiration the diaphragm was the chief factor in fluctuations of the intra-abdominal pressure. Consequent on the greatly increased muscle tension incident to asphyxia, a marked rise in intra-abdominal pressure was observed and sustained until terminal muscular relaxation occurred, when the pressure fell.

Helen Coombs<sup>6</sup> (1922) stressed the importance of the reflex tonicity of the abdominal musculature in determining intra-abdominal pressure. She referred to this factor as "postural activity." She found that when the abdomen of the cat is gradually distended with saline solution, a reflex lengthening of the abdominal muscles occurs, so that a considerable volume of fluid can be introduced without altering the intra-abdominal pressure. After about 500 cc. of fluid has been allowed to run in, a point is reached at which a sudden increase in intra-abdominal pressure occurs. She referred to this as the critical pressure. It is usually observed when enough fluid has run in to make the respiration markedly costal in character.

The effect of increased intra-abdominal pressure, as produced in experimental ascites on the blood pressure, has also been the subject of considerable study. Henriëus<sup>7</sup> (1890) observed that an increase of intra-abdominal pressure in cats or guinea-pigs of from 27 to 40 cm. of water was fatal due to the inhibition of respiration by interference with thoracic expansion. Hamburger<sup>8</sup> (1896) found that an increase of intra-abdominal pressure up to 25 cm. of water (18.5 mm. of Hg) caused a rise of from 10 to 15 mm. of Hg in the arterial pressure. Increase of the intra-abdominal pressure above 25 cm. of water caused a fall in arterial pressure. Hamburger also found that pressures of from 40 to 45 cm. of water would cause death of the animal about by heart failure.

Emerson also found that intra-abdominal pressures normal in the experimental animal caused a fall in arterial pressure.

5 Wagoner, G. W. Negative Intra Abdominal Pressure. *Ann. I. M. S.* **171**: 697, 1926.

6 Coombs, Helen C. The Mechanical Aspects of Intra-abdominal Pressure. *Am. J. Physiol.* **61**: 159, 1922.

7 Henriëus, G. Ueber den Einfluss der intra-abdominalen Druckes auf die Respiration. *Ztschr. f. Biol. Chem. u. Physiol.* **8**: 117, 1890.

8 Hamburger, H. J. Ueber den Einfluss der intra-abdominalen Druckes auf die Allgemeine Arterielle Blutdruck. *Arch. f. Anat. u. Physiol.* **1896**.

## PAST PRESIDENTS

- 1918 SAMUEL J MELTZER, New York
- 1919 WILLY MEYER, New York
- 1920 WILLY MEYER, New York
- 1921 RUDOLPF MATAS, New Orleans, Pa
- 1922 SAMUEL ROBINSON, Santa Barbara Calif
- 1923 HOWARD LILIENTHAL, New York
- 1924 CARL A HEDBLUM, Chicago, -Ill
- 1925 NATHAN W GREEN, New York
- 1926 EDWARD E ARCHIBALD, Montreal, P Q
- 1927 FRANZ TOREK, New York

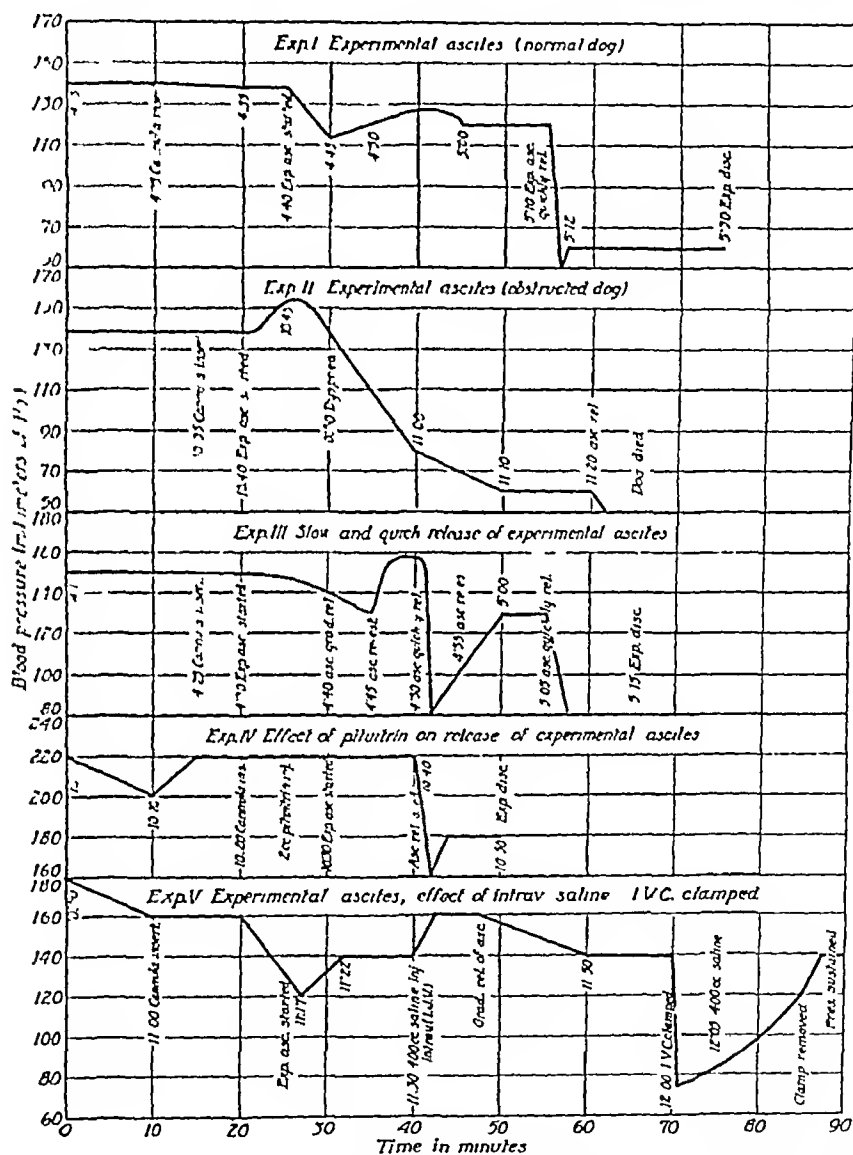
## PAST SECRETARIES

- 1918-1922 NATHAN W GREEN, New York
- 1922-1924 CHARLES GORDON HEYD, New York
- 1924-1928 ETHAN FLAGG BUTLER, Sayre, Pa

## MEETING DATES

- 1918 CHICAGO, June 10
- 1919 ATLANTIC CITY, N J , June 9
- 1920 NEW ORLEANS, May 1
- 1921 BOSTON, June 6
- 1922 WASHINGTON, D C , April 29
- 1923 CHICAGO, May 28
- 1924 ROCHESTER, Minn , June 5
- 1925 WASHINGTON, D C , May 4
- 1926 MONTREAL, P Q , September 30
- 1927 NEW YORK, May 9

occasionally employed. This increase in the intra-abdominal pressure was usually accompanied by a fairly well marked dyspnea. After the intra-abdominal pressure had been sustained at the new level for some time, the abdomen was suddenly decompressed in three normal dogs by quick incisions. In all the animals, a marked immediate fall in blood pressure occurred. However, a fatality was not brought about by this



Blood pressure tracings illustrating the effect of sudden release of an increased intra-abdominal pressure on the arterial pressure (I and II), and factors that modify this effect (III, IV, V)

sudden release of the intra-abdominal pressure in the normal dog. Following the sudden decompression of the abdomen in one animal (first tracing), a rise in the arterial pressure did not occur during the next twenty minutes of observation. In the other two animals, the pressure

has been made, this is replaced by the surgeon's fingers, if they are not too large. This extreme care in making the dissection must be continued till the pleura has been detached beyond the rib above and beyond the rib below the intercostal space, after which McBurney retractors may be inserted, care being taken that the pleura is not pinched by them. Before exerting any traction on the two ribs, one should make sure that the pleura is detached well beyond the anterior and posterior ends of the intercostal incision, as the pleura would be torn at those places if the ribs were drawn apart while it is still attached to them in front and behind. The continuation of the procedure of detaching the pleura becomes much easier now, when retraction is used and the fingers can be more easily introduced. When the pleura has been detached from the seventh and sixth ribs posteriorly, the seventh rib may be divided near the spine. This gives a great deal more space for the hand to continue the detachment higher up. When the fifth rib has been cleared, the sixth rib may be cut in the line of the posterior vertical incision, care being taken not to injure the pleura with the bone shears. The stripping of the pleura being continued farther upward, the fifth and fourth ribs may then be divided without danger of injuring the pleura. The rib spreader is introduced with caution so that its flanges do not catch the pleura anywhere. The separation of the pleura from the thoracic wall is continued till the entire costal pleura, from the apex to the diaphragm, has been detached, after which it is also separated from the spinal column, the aorta and the diaphragm. The detachment of the costal pleura is not difficult, except at the beginning, as has been mentioned. In one case, the patient detached his own pleura over a large area by a sudden, deep inspiration while he was going under the anesthetic, the skin and muscle incision having been made by paravertebral and regional block. It occurred so quickly, with a tearing sound, that my first thought was that he had made a rent into his pleura causing collapse of the lung, close examination, however, showed the pleura to be uninjured and in close contact with the partially collapsed lung. The task of detaching the pleura is more difficult where it covers the spinal column and the diaphragm. There the attachment is much firmer, and the separation requires some patience. The mediastinum is reached after the separation of the pleura has been continued mesially beyond the lateral wall of the aorta, and there the esophagus will soon be brought in evidence.

It is rather remarkable that so extensive a stripping of the pleura is practically bloodless. The lung collapses and sinks out of the way just as it does in the transpleural operation, except that the collapse is more gradual, keeping pace with the separation of the pleura. The exposure of the esophagus is as complete as in the transpleural operation, and the view is almost identical in gross appearance, for the parietal pleura, which has been separated from the wall of the chest, lies in close apposition with the lung and would be taken for its own visceral pleura unless closely examined.

The operation of resecting the esophagus is the same as in my method of transpleural resection,<sup>1</sup> the essential steps of which are the

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1 Torek, Franz. *Ann Surg*, April, 1915

of regularity. The potential for such an occurrence, however, exists and should be borne in mind. Two instances in which this phenomenon was observed are cited.

In most instances, when surgical intervention becomes necessary in the distended abdomen, the enlargement has been present for a long time. As has been pointed out, the intra-abdominal pressure in such instances is not actually increased greatly, owing to the stretching of the abdominal walls incident to the expansion of the abdomen. This situation is well illustrated in the pregnant abdomen. If such a readjustment did not already obtain, the sudden opening of the abdomen and uterus in cesarean section would be followed regularly by circulatory collapse.

Only in animals previously ill (in which duodenal obstructions had been present for two days) did a sudden release of the increased intra-abdominal pressure result fatally. In normal animals, a marked fall in arterial pressure occurred when the distended abdomen was quickly opened. A gradual return of the arterial pressure to the normal level usually followed. This occurrence could be obviated by a gradual release of the ascites, and it could be inhibited in large measure by the previous subcutaneous administration of solution of pituitary and in a lesser degree by the previous intravenous injection of saline solution. After this sudden circulatory adjustment had been brought about, increasing the intra-abdominal pressure again by approximating the edges of the incision and filling the abdomen with fluid, the intravenous infusion of saline solution or the administration of solution of pituitary hastened the return of the arterial pressure to the normal level.

#### PROTOCOL OF EXPERIMENTS <sup>10</sup>

EXPERIMENT 1 (April 18, 1927).—Experimental ascites in normal dog. The tracing was started at 4 15. The blood pressure was 140 mm. A cannula was inserted into the abdomen at 4 25. Blood pressure at 4 35 was 138 mm of mercury, at 4 40, it was the same. At this time the ascites was started. A water pressure of about 50 cm (37 mm of mercury) was employed. Following the increased intra-abdominal pressure there was a slight drop in the blood pressure to 114 mm at 4 45. At 4 50, the pressure had gradually risen to 120 mm and at 4 55 to 140 mm, with a gradual fall to 120 mm at 5 00. At 5 10, the pressure was still 120 mm. At this time, the ascites was quickly released by a stab wound of the abdomen and the arterial pressure suddenly fell to 50 mm. At 5 12, it had risen to 60 mm. It sustained itself at this level until the experiment was discontinued at 5 30.

EXPERIMENT 2 (April 20, 1927).—Experimental ascites in dog, with duodenal obstruction of two days' standing. The tracing was started at 10 20. The blood pressure was 138 mm. A cannula was inserted into the abdomen at 10 35. The blood pressure was the same. At 10 40, experimental ascites was begun, a water pressure of about 45 cm of water (33 mm of mercury) being used. Following this there was a gradual rise of arterial pressure to 160 mm of mercury.

<sup>10</sup> The details of the remaining experiments are omitted.



branches of the aorta had to be divided at the arch. The tumor was adherent to the right pleura, from which it could not be separated, therefore the liberation of the tumor necessitated opening the right pleura. The esophagus was divided below the tumor, the lower stump was invaginated and the upper one brought out at the neck, where it



Fig 2—Roentgenographic appearance of chest the second day after Torek's extrapleural esophagectomy had been performed, attack from left side. The division of four ribs can be made out, though the lines are rather faint, owing to the perfect alignment of the cut ends. The chest is seen to be normally transparent on the side of the operation, whereas the right pleura, which was opened at operation, shows a haze.

was sutured. A cigaret drain was placed through the length of the mediastinum and was led out at the ninth space. The chest was then closed.

# THIRTY-FOURTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY \*

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## CONGENITAL DEFORMITIES

*Congenital Dislocation of the Hip*—Willard<sup>1</sup> reviewed the results of reduction by the Davis method in twenty cases of congenital dislocation of the hip five years after operation. Six of the patients showed bilateral dislocations. Reports were made on twenty-six hips. The results were: Ten per cent failure, both bilateral dislocations, 30 per cent, reduced but unstable, 60 per cent of good functional results in all single dislocations. In studying the 30 per cent of the cases in which the dislocations were reduced but unstable, Willard felt that much of the change that takes place in the head and acetabulum after reduction is due to injury at the time of reduction. From this he advocated reduction (closed) before weight-bearing begins, if possible. Reduction should be accomplished by the gentlest sort of manipulations. The type of manipulation is of less importance than the amount of skill with which it is used. Open operation should be resorted to if manipulation fails.

Eikenbary<sup>2</sup> reported a congenital bilateral dislocation of the hip which was reduced by open operation when the child was 11, the patient was seen again at the age of 23. The operation consisted of enlargement of the acetabulum by means of a chisel and a heavy curet. The result thirteen years later was satisfactory, with 90 degrees motion in

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\* This Report of Progress is based on a review of 166 articles selected from 419 titles dealing with orthopedic surgery appearing in medical literature between March 12, 1927, and July 2, 1927. Only those papers that seem to represent progress have been selected for note and comment.

1 Willard, Deforest P. *J Bone & Joint Surg* 9 270 (April) 1927

2 Eikenbary, C F. *Northwest Med* 26 161 (March) 1927

# EXPERIMENTAL ABSCESS OF THE LUNG IN THE DOG\*

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The American Association for Thoracic Surgery has done much to stimulate an interest in the etiology and methods of prevention of post-operative abscess of the lung. Tonsillectomy and other operations in the upper air passages that are carried out under general anesthesia are responsible for the largest number of the reported cases, but abscess of the lung does occur as a complication of tonsillectomy and extraction of teeth under local anesthesia and occasionally after appendectomy. It is true that a real abscess in the lung with cavity formation commonly follows an operation for a septic condition, but in studying the etiology of this type of abscess it might be well to consider the relation between post-operative bronchopneumonia (a complication in about 5 per cent of clean surgical operations, such as hernia) and infections of the lung that proceed to cavity formation. Are all abscesses of the lung due to infected emboli from the vessels surrounding the operative field, or is the aspiration of mouth secretions, bits of infected tissue and the plugs of detritus from the crypts of tonsils the common method of post-operative lung infection? Are the clinical and pathologic differences between bronchopneumonia, massive collapse of the lung and lung abscess determined by different routes of infection or by the type of the infecting organism and the resistance of the patient? These are questions that we are not prepared to answer, but they deserve consideration in the study of postoperative complications in the lung. The removal of tonsils under general anesthesia is the most talked-of cause of abscesses of the lung. Cutler and his associates, Holman and others ascribe these abscesses to the liberation of infected emboli, but our experience during the past twelve years at the Johns Hopkins Hospital, where 3,500 patients have had their tonsils removed under ether anesthesia without the occurrence of a single postoperative abscess of the lung, leads us to believe that aspiration is the cause of this complication. In each of these 3,500 patients the following safeguards against aspiration have been employed: 1 Hypodermic administration of morphine sulphate and atropine is employed about thirty minutes before the operation. 2 The anesthetic is administered by a trained anesthetist. 3 During the operation, the head of the patient is at least 15 inches lower than

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following conclusions 1 Coxa valga may occur without a displacement of the head, but through an insufficiency of the roof of the acetabulum, as in many spastic patients and in those with coxa valga luxans 2 Displacement of the head does not necessarily produce coxa valga 3 The displacement of the head can occur only when a pathologic process involving the epiphyseal line coexists, and in such a case, if a deficiency of the acetabulum is also present, coxa valva may develop. Eitton<sup>6</sup> concluded that various factors may play a part in the production of coxa valga.

*Osteochondritis of the Vertebral Body*—Buchman<sup>6</sup> described five cases in children who had disturbance of the spine which he believed belong to the class of cases already described, he attempted to draw a line between these cases and the cases of so-called vertebral epiphysitis. He considered the first a disease of one of the primary centers of ossification and the second a disease of one of the secondary centers. The age of the patient thus determines the type of lesion. Buchman gave as his view of the cause of these conditions the fact that they are due to an increase in static demand, going hand in hand with a decrease in static capacity. He discussed slipping epiphyses in the same relation but finally admitted that one seldom sees these conditions in infantile paralysis and infantile rickets, in which the "capacity" of the bone is obviously decreased.

[ED COMMENT—We do not see that Buchman's theory adds to the discovery of the causation of the condition. The essence of Wolff's law is that "static capacity" increases in proportion to "static demand." When the reverse is true, there is gross evidence of a pathologic disturbance, and the cause must be sought.]

#### NUTRITIONAL DISEASES OF THE BONE

*Rickets*—Investigations by Grayzel and Miller<sup>7</sup> tended to confirm the view that difficulty in intestinal absorption of calcium and phosphorus may be responsible for the abnormalities in metabolism of these elements which are found in rickets. Their studies showed that with a normal diet the reaction remained acid with considerable constancy at different levels of the gastro-intestinal tract. High variations in fat, protein, or carbohydrate did not cause notable changes. The rickets-producing diet did, however, cause a definite rise in the  $p_H$  of the intestinal contents, even to the point of alkalinity. Ultraviolet radiation or the administration of cod liver oil to dogs on the same diet caused an acidification of the contents to within the normal range.

6 Buchman, Joseph J. *Bone & Joint Surg* 9:55 (Jan.) 1927

7 Editorial, *J A M A* 88:1715 (May 28) 1927

some of the pus from the chronic suppuration in the frontal sinus flowed into the trachea, probably during sleep, and produced the isolated abscess in the lower lobe on one side. This supposition is supported by the demonstration with dark-field illumination of spirochetes in the frontal sinus after six weeks and in the lesion of the lung. Many other organisms could be seen in the smear from the abscess of the lung, but it is worthy of note that the Vincent bacillus was not found.

We have mentioned before that we succeeded in producing a chronic abscess of the lung only after two years of effort. In the fifty experiments made during these two years, we introduced, through the bronchoscope, pieces of cotton soaked with virulent cultures of pneumococcus, staphylococcus, several varieties of streptococcus, the colon bacillus and various types of fungi. Our results with these organisms were either negative or resulted in a diffuse infection of the lung, and are in accord with those of Cutler, Holman and others. It is striking, however, that the same procedure will result in a localized, chronic suppuration of the lung when the scrapings from pyorrhea cavities are used as the infecting agent. We realize fully that it cannot be inferred from these experiments on animals that the aspiration of spirochetes from the mouth is the cause of postoperative abscess of the lung in man, but this experimental observation is suggestive and shows the specificity of organisms. David T. Smith<sup>1</sup> of Ray Brook, N. Y., has been able to produce pulmonary abscesses in mice, guinea-pigs and rabbits by intra-tracheal injection of material from pyorrhea cavities. This same group of organisms is normally present in the material expressed from crypts in the tonsils. It has been known for many years that the foul odor of the sputum from a chronic abscess of the lung is due to spirochetes and that the intravenous administration of one of the arsenic compounds is of value in such cases. The spirochetes in the mouth have been regarded as secondary invaders, but it is possible that they may play an important rôle in the etiology of abscess of the lung which follows operations on the tonsils and teeth.

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<sup>1</sup> Smith, David T. Experimental Aspiratory Abscess, Arch Surg **14** 231 (Jan) 1927

malacia started when the patient was 20, under the form of genu valgum, for which Berger performed an osteotomy. The decalcification progressed rapidly during the first two years and then stopped for a while. In 1905, the patient's health was better, the pains had disappeared, and it was possible to perform motions with the right hand. The roentgenograms showed beginning recalcification. The remission lasted until the time of death, and this is the only reported case in which this has ever occurred. Between 1896 and 1905, the examinations of the urine showed tremendous elimination of calcium, often from 9 to 10 Gm. Autopsy showed that all the bones were twisted and deformed. Concretions that had been discovered sixteen years earlier by Berger during the active stage of the disease were found in the left renal pelvis. No change was discovered in any of the glands of internal secretion except the suprarenals, both of which were enlarged, the left one weighing 30 Gm.

#### TUBERCULOSIS

*Tuberculosis of the Knee and Hip*—Hibbs<sup>12</sup> studied the end-results in a group of cases of tuberculosis of the knee and hip in which the patients were treated by conservative measures. The diagnosis was incorrect in 30 per cent of the patients with tuberculosis of the knee, of the 67 remaining patients, 7 died from other forms of tuberculosis, and in 43 the disease became quiescent. In 16 of the latter, the disease again became active at a later period. Two hundred and eight patients had tuberculosis of the hip. The error in diagnosis was 22 per cent. Of those who probably had tuberculosis, 24 per cent died, of the 114 remaining, 17 still had active tuberculosis. In two, the disease was quiescent with free motion, and in four it was quiescent with marked limitation of motion. Fifteen patients had relapses after periods of quiescence varying from one to nine years. In the cases in which operation was performed, the results were better. Sixteen of the knees mentioned were fused, and all of these patients remained free from symptoms. The hip had been fused in more than 80 cases, and the results thus far obtained give promise of a high percentage of cures. Hibbs emphasized the point that diagnosis must be made by tests performed in the laboratory, and that many statistical studies are inaccurate because of errors in diagnosis.

*Occurrence of Foci in the Bones in Tuberculous Joints*—Koenig<sup>13</sup> pointed out the impossibility of determining the presence of foci in the bone in tuberculous joints by means of roentgenograms. Riedel reported finding foci present in the bones in more than 70 per cent of

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12 Hibbs, Russell A. *Southern M J* 20 278 (April) 1927

13 Koenig, Fritz. *Zentralbl f Chir* 54 1030 (April 23) 1927

## PREVIOUS INVESTIGATIONS

Clinical studies of the etiology of the various types of abscesses of the lung have indicated the probability that most of them are aspiratory in origin. Experimental results in animals, however, have not supported this.

The clinical studies of Richardson,<sup>1</sup> Scudder,<sup>2</sup> Whittemore,<sup>3</sup> Moore,<sup>4</sup> Singer and Graham,<sup>5</sup> Cutler and Schlueter,<sup>6</sup> Hedblom,<sup>7</sup> and numerous other investigators have revealed the fact that a considerable percentage of all nontuberculous abscesses of the lung follow operative procedures about the upper respiratory tract. There is, at least in this group of cases, ample opportunity for the aspiration of infectious material, and this opportunity is soon followed by the development of the abscess. Cutler found that 29 per cent of 1,908 cases of abscess of the lung followed operations, half of which were tonsillectomies.

The larger group of abscesses of the lung which do not follow operative procedures, about 65 per cent of all cases, has not received the close study that the postoperative group has had. The group of cases to be reported in this paper shows that most of this group of abscesses of the lung apparently follow infections of the respiratory tract.

The experimental production of abscess of the lung has been difficult. Kline<sup>8</sup> and Smith<sup>9</sup> have succeeded in producing acute aspiratory abscess by the insufflation of the bacteria obtained from the teeth. Cutler and his co-workers, Homan,<sup>10</sup> Schlueter<sup>6</sup> and Weidlein<sup>11</sup> have

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1 Richardson, C. W. Tonsillectomy with Consideration of Its Complications, *Wash. M. Ann.* **12** 2, 1912.

2 Scudder, C. L. A Report of the Cases of Lung Abscesses at the Massachusetts General Hospital Clinic, Boston *M. & S. J.* **171** 523, 1914.

3 Whittemore, W. The Etiology and Treatment of Non-Tuberculous Pulmonary Abscess, *Surg. Gynec. Obst.* **38** 461, 1924.

4 Moore, W. F. Pulmonary Abscess—An Analysis of 202 Cases following Operative Work about the Upper Respiratory Passages, *J. A. M. A.* **78** 1279 (April 29) 1922.

5 Singer, J. J., and Graham, E. A. A Study of Thirty-Four Cases of Abscess of the Lung, *J. A. M. A.* **83** 193 (July 21) 1923.

6 Cutler, E. C., and Schlueter, S. A. The Experimental Production of Abscess of the Lung, *Ann. Surg.* **84** 256, 1926.

7 Hedblom, C. A. The Surgical Treatment of Acute Pulmonary Abscess and Chronic Pulmonary Suppuration, *J. A. M. A.* **83** 1577 (Nov. 15) 1924.

8 Kline, B. S. Experimental Gangrene, *J. Infect. Dis.* **32** 481, 1923.

9 Smith, David T. Experimental Aspiratory Abscess, *Arch. Surg.* **14** 231 (Jan.) 1927.

10 Homan, E., Weidlein, I. F., and Schlueter, S. A. A Method for the Experimental Production of Lung Abscess, *Proc. Soc. Exper. Biol. & Med.* **23** 266, 1926.

11 Schlueter, S. A., and Weidlein, I. F. Postoperative Lung Abscess. An Experimental Study, *Arch. Surg.* **14** 457 (Feb.) 1927.

## OSTEOMYELITIS

*Acute Hematogenous Osteomyelitis*—Robertson<sup>16</sup> produced experimental osteomyelitis in animals and reviewed the literature. He believed that the experimental work proves beyond any doubt that 1. Organisms introduced into the blood stream are deposited, among other places, in the long bones. 2. In bone, active phagocytosis is present, except in the metaphyses. 3. Organisms produce inflammatory centers in metaphyses independent of trauma. 4. It is impossible to produce a general infection of the medulla by a simple inoculation of organisms into the blood stream. 5. Trauma may determine a local infection. 6. Growing bones develop abscesses of the osteomyelitic type within them, adult bones do this rarely.

Robertson tried to correlate these observations with the clinical picture of osteomyelitis. His conclusions were as follows: 1. Staphylococcal infections come from lesions of the skin by contamination of the blood. 2. The primary lesion of the bone in man is determined by trauma. 3. Continued septicemia favors the formation of supplementary lesions of the bone. 4. The lesion of the bone is in the metaphysis of the growing child. 5. The chief symptom is pain, the chief sign tenderness over the involved metaphysis. 6. Treatment consists of early operation into the metaphysis for the purpose of drainage.

Wilensky<sup>17</sup> described the mechanism of acute osteomyelitis as, first, a bacteremia or general infection of the blood, second, the development of a fixation point in the vascular network of a bone (thrombo-embolic phenomenon), third, the development of a pathologic process characterized by thrombo-arteritis or thrombophlebitis, and fourth, the resulting necrosis of bone cells and tissue. He believed that the severity of the general infection may be determined by plating the blood cultures and counting the colonies. If bacteremia is not present, the prognosis is good. If many colonies are found, the infection may be of the acute fulminating type and there are practically no chances of help by operation. Between these two extremes is a large group of cases in which demonstrable bacteremia and one or more foci of osteomyelitis are present. If operation is performed early in these cases, the prognosis is good. If the bacteremia is severe, the operation must consist in radical removal of the thrombophlebitic focus.

*Treatment of Chronic Osteomyelitis*—According to Thornton<sup>18</sup> there are operable and inoperable stages of chronic osteomyelitis. Following the acute stage, all patients go through an inoperable phase. The operable stage is reached when new bone shadows have become dense

16 Robertson, D. E. *J. Bone & Joint Surg.* 9:8 (Jan.) 1927.

17 Wilensky, A. O. *Ann. Surg.* 85:428 (March) 1927.

18 Thornton, Lawson. *J. Bone & Joint Surg.* 9:294 (April) 1927.



French, was moistened with sterile water and gently introduced deep into the respiratory tract. A small, dry, sterile basin was partly immersed in a larger basin of water at 40 C (104 F). The two basins were placed on the floor at the head of the anesthetized animal. A sterile 5 cc syringe was also immersed in water at 40 C. The patient was instructed to lean forward over a chair and to expectorate pus, which was coughed up into the small, warm basin. This pus was immediately aspirated into the warmed syringe, and 3 cc was injected into the bronchus through the previously placed catheter. Not more than thirty seconds elapsed between expectoration and instillation of the pus. The animal was placed in a comfortably heated room.

Feb 20 The dog was very lively, it ate and played

Feb 21 The condition did not change

Feb 23 The dog was active and leaped to greet us. There was no cough or rales, a roentgenogram did not show a shadow.

Feb 25 Maltese was not apparent. A roentgenogram did not show a shadow.

Feb 27 The dog was not so active in the morning. His temperature was 101 F. A roentgenogram did not show a shadow. There were no rales or dyspnea.

Feb 29 The dog was less active than at any previous time, but auscultation or percussion of the chest did not reveal any sign of abscess.

March 5 There were no physical signs of abscess. The dog looked haggard and was losing weight. He did not cough.

March 8 The dog did not cough and continued to lose weight.

March 11 The animal was markedly emaciated. He did not cough.

March 13 The dog was very emaciated and inactive. He did not cough. A roentgenogram showed mottling in the right side of the chest, but no abscess cavity.

March 14 The dog was found dead in the cage.

*Autopsy*—The pleural cavities did not contain fluid or pus. The right middle lobe was firm, but crepitant. Several small yellow areas presented themselves along its costal surface. The trachea was clamped, and the lungs were removed en masse. A longitudinal incision was made into the trachea, and it was found to contain about 3 cc of moderately viscid, yellow pus. The bronchus to the right middle lobe was filled with air containing pus.

The lungs were inflated through a cannula, and at the same time a roentgenogram was taken. Abscess cavities were not visible, but a dense portion of the lung could be made out. The gross and microscopic examination of the middle lobe was far more conclusive of the presence of multiple abscesses than the roentgenographic examination. The cut surface of the right middle lobe is shown in figure 2.

*Microscopic Examination*—Many areas were filled with polymorphonuclear leukocytes and fewer round cells. The alveolar epithelium was absent. These areas of necrosis and pus contained small bubbles of air and non-necrotic alveolar epithelium was found between them. Atelectasis was not marked in these areas. In many places, the remains of a bronchiole could be seen near the center of the abscess. Figure 1 shows one such bronchiole in which the epithelial lining has been eroded and only the fibrous tissue of the wall is intact. Epithelial casts can be seen clinging to the fibrous tissue ring. The infectious process penetrates the wall of the bronchiole at one place. Bacteria can be seen throughout the wall of the bronchiole and surrounding tissue, but bacteria were not found in the walls of the blood vessels or inside the vessels themselves. Spirochetes were not found.

pendently of spinal drainage. The results in the patients treated by others are in agreement with our results in this and in previous studies as regards mortality rate, incidence of residual paralysis, and bedside impressions concerning early good effects of the serum. The number and variety of the patients treated are sufficient, and control observations are adequate to justify the conclusion that this poliomyelitis antistreptococcus serum is of value in the treatment of acute anterior poliomyelitis. The serum used possessed the power of neutralizing the toxic material contained in cultures of streptococcus as measured by intracutaneous injection, it diminished the infective power in vitro of the streptococcus as measured by intracerebral injection, and it cured rabbits inoculated intravenously with the streptococcus, properties not possessed by horse serum. Some of the batches of serum neutralized the virus in vitro, and protected monkeys against poliomyelitis in the forced experiment by intracerebral inoculation of virus. Rabbits have been immunized against intracerebral inoculation of the streptococcus by the methods used in the preparation of the serum in horses, hence the curative action noted clinically would seem attributable to the specific antibodies contained in the serum and not to nonspecific or foreign protein effects.

[ED COMMENT—Rosenow failed to convince many competent bacteriologists that the streptococcus which he has isolated from patients with poliomyelitis bears any causal relation to that disease. Hence we hesitate to accept the conclusion that antistreptococcus serum is of specific benefit in the disease. While the results reported are suggestive, whether or not they are conclusive will have to be left to the judgment of more competent authorities. When patients are reported as having been treated with serum, it will be important to specify whether convalescent serum or Rosenow's serum has been used.]

#### ARTHRITIS

*Specific Causative Factors*—Hadjopoulos and Burbank<sup>21</sup> employed immune serum in order to determine by the reactions the types of infective organisms in cases of chronic multiple arthritis, they checked these by cultures from various foci of infection which had been discovered. They believed the streptococcus to be the main causative factor in both of these sources. By neutralization of the alexin in freshly drawn blood of arthritic patients, they were able to grow pure cultures of various organisms, streptococci, diphtheroids and *Staphylococcus aureus*. Taking the streptococci thus isolated, they were able to produce arthritic symptoms in animals by inoculating the blood with those organisms.

[ED COMMENT—Careful bacteriologic investigations have been made of chronic arthritis, usually with inconclusive results. The observations reported require confirmation.]

<sup>21</sup> Hadjopoulos, L. G., and Burbank, Reginald. J. Bone & Joint Surg. 9: 278 (April) 1927.

in the lung of a human being. The lesions were produced in healthy dogs in which opportunity for pulmonary embolism had not been established. Regarded both from the experimental and from the clinical point of view as well as microscopically, the abscesses were abscesses of the lung produced by aspiration.

An analysis of the twenty-one experiments in series II revealed the following significant facts. The animals in fifteen experiments failed to develop abscess of the lungs, and only three animals in the total twenty-one experiments developed abscesses. Each animal had received fresh, warm pus from patients with chronic abscess of the lung. Some of the animals which did not develop abscesses had received



Fig 2—Cut surface of lung containing abscesses. *A* indicates the abscesses which are remote from the main bronchus, *B*, the bronchus. The infectious material seems to have been trapped in the smaller bronchioles.

exactly the same amounts of the same pus and at almost the same minute as other animals that did develop abscess. Why did some of these animals develop abscess of the lung while others did not? Why does one patient develop a postoperative abscess of the lung while a second patient on whom a similar operative procedure has been carried out does not?

An examination of the lungs of those animals in which multiple abscesses had been produced by aspiration seemed to indicate an answer. Most of the abscesses were situated in those portions of the lung farthest removed from the main bronchus (fig 2). The infectious material must have been *trapped* in the smaller bronchioles and alveoli.

following the disappearance of intestinal symptoms. The aspirated fluid from the knee contained a large number of polymorphonuclear cells, but neither on microscopic study nor on cultures could any bacilli be found. Agglutination tests of the fluid proved positive for Shiga and Flexner bacilli and negative for Hess and colon bacilli. The results were the same in another patient with arthritis who had had diarrhea two weeks before. Besson and Ehringer concluded that the agglutination test is of value in differentiating this type of arthritis.

*The Protozoan Theory of Arthritis*—Barrows and Armstrong<sup>24</sup> discussed in detail the protozoan etiology of chronic deforming arthritis. In a series of 209 cases, 171 patients received medical treatment alone in which antiparasitic therapy played the chief rôle. From the clinical standpoint the results were considered satisfactory benefit being claimed in 93 per cent of the cases.

[ED. NOTE—Conclusive proof of the etiologic relationship of protozoa to arthritis has not yet been presented.]

*Blood Calcium and Phosphorus in Arthritis*—Nachlas<sup>25</sup> studied the level of calcium and phosphorus in the blood in arthritis. The reports in the literature on this subject show lack of agreement some observers claiming an increase and others no change. Nachlas' studies are in accord with the latter group. He was unable to demonstrate any change in blood calcium or blood phosphorus in either type of arthritis.

#### PAIN IN THE BACK

*Injuries of the Back in Industrial Employees*—Herndon<sup>26</sup> made a study of 941 consecutive cases of injury of the back among industrial employees, and his report gave an idea of the relative frequency of the various types of injury. Fifty-three per cent of the injuries were classified as sprains and of these two-thirds were in the lumbosacral region. Forty-one of the patients, or 4 per cent, had fractures of the vertebral processes, the transverse processes being injured in thirty cases. There were thirty cases of fracture of the vertebral body. Only one third of these showed involvement of the cord. Arthritis neurosis, malingering and other diseases accounted for the remaining cases. In conclusion Herndon stated that "the most frequent causes of unsatisfactory progress are failure to report the injury early to make a complete examination and diagnosis at once to prescribe efficient treatment, and to follow up this treatment."

24 Barrow, J. V., and Armstrong, E. L. *California & West Med* 26:322 (March) 1927.

25 Nachlas, I. W. *J. Bone & Joint Surg* 9:37 (Jan.) 1927.

26 Herndon, Richard F. *J. Bone & Joint Surg* 9:234 (April) 1927.

The lobe appeared solid, and beneath the pleura were many dark, yellow, indurated areas. The cut surface of this lobe showed many small abscesses, the bronchioles were filled with chocolate colored, foul pus. There were no large abscess cavities.

The right middle lobe was adherent to the surrounding lobes. Its tip projected stiffly and maintained its position beside the heart, while the right lower and upper lobes were collapsed. The right middle lobe was studded with yellow, indurated areas, with air-containing, crepitant lung tissue between them. Between the right lower lobe and the vertebral ridge, an intrapleural abscess was opened which contained about 10 cc of putrid, foul-smelling, chocolate-colored, granular pus. This was like the original pus from the patient both in color and in odor. Smears and cultures showed a fusiform bacilli and spirochete flora identical with that in the original pus. The trachea was clamped off and the lungs removed en masse.

The trachea and bronchi were lined with chocolate-colored, foul-smelling pus in which many small, cheesy, yellow masses were found. The bronchi to the right middle lobe and to the mediastinal lobe were filled with foamy pus. Incision along the bronchus to the middle lobe revealed the silk ligature hanging free in its lumen and attached by only a small section of its wall. The lumen of this bronchus was now patent—the ligature which was placed around it twenty-six days previously had cut through its wall. The smaller bronchioles which empty into this bronchus to the right middle lobe exuded pus when slight pressure was made on the external surface of the lobe. There were multiple small abscesses, varying from less than 1 mm to 8 mm in diameter, throughout the entire lobe. There were no large air-containing abscess cavities. The abdomen did not contain pus.

*Microscopic Examination*—Bacteriologic. Smears from the bronchioles of the right middle lobe, from the mediastinal lobe, and from the trachea showed an identical bacterial flora. Cocci, fusiform bacilli and spirochetes were present in a profusion. The yellow granules swarmed with spirochetes—dozens were present in each oil immersion field. Cultures showed *Diplococcus melanogenticum*.

*Pathologic*. The sections showed that in certain areas the alveoli were replaced by a solid mass of polymorphonuclear and round cells. Here the alveolar epithelium was entirely absent. In places, many of the alveoli were still outlined by capillaries containing intact red blood cells. The blood vessels were still patent in the sea of pus (fig 3). There were no emboli, even in the smaller capillaries. The bronchioles were filled with pus, and in many places the epithelial lining of the bronchioles was missing.

This experiment was repeated, warm minced tonsil being used instead of pus from the abscess. The crypts of the tonsil contained myriads of spirochetes. Fusiform bacilli and cocci were also present. The animal pursued the same postoperative course as the first animal, except that the thoracotomy wound did not break open and he did not cough. This animal showed malaise at the end of the ninth day after injection.

The second animal was killed on the twenty-first day. Multiple abscesses were found in the right middle lobe. The bronchus to this lobe had also reestablished the patency of its lumen, the silk ligature having cut through its walls. At autopsy, yellow granules containing myriads of spirochetes were found in the pus in the bronchus to the right middle

tion He summarized these changes as follows The vitality of the artery was much altered, the contractile elements were replaced by connective tissue The changed nutritive conditions led to the deposition of fat within the endothelial cells The muscles lost their characteristic staining reaction and showed distinct signs of necrobiosis Fifty days after the operation, the lumen of the collateral vessels was wider than on the normal side and the media was hypertrophied From a consideration of these changes the author pointed out the inadvisability of performing the operation in cases in which the vessels have been altered in such a way as to lose their elasticity

*Oscillometry in Circulatory Disturbances of the Extremities.*—Samuels<sup>37</sup> described the oscillometer of Pachon and discussed its use in studying various arterial disturbances in the extremities He concluded that it is a valuable adjunct and should be used as a part of the general physical examination in any case in which circulatory disturbance is suspected It is of value in the diagnosis of early occlusive disease of the peripheral arteries and in the differentiation of neurogenic from organic arterial disease By its aid, the progress of arterial disease in the extremities can be studied quantitatively The instrument exhibits certain physical limitations, such as its inability to select any one vessel for study and its insensitivity to that state of the circulation represented as lying between the zero point of the instrument and the total cessation of arterial outflow

*Results of Suprarenalectomy in Spontaneous Gangrene of the Extremities*—Seneque<sup>38</sup> summarized the report of an investigation by Herzberg, a Russian surgeon of the results of suprarenalectomy Herzberg was able to collect reports of 112 cases, including 58 cases of Oppel (who, in 1921 published the theoretical basis for the operation), 6 cases of Leriche, 8 personal cases, and the rest representing the cases of various Russian surgeons Of the 112 cases a cure (meaning complete disappearance of pain with cicatrization of the ulcers) was obtained in 14 cases However these so-called cures have not existed for a sufficient period of time as yet Gangrene is of slow evolution In a great many cases, there was a complete disappearance of pain directly after operation the ulcers cicatrized and the arterial pulse reappeared But remote observations show that the improvement was only transient A minimum of two years during which symptoms do not appear is needed before one may speak of cure Applying this test, the author found only 3 cures in 112 cases and even here it could not be proved that the cures resulted from the operation Com-

37 Samuels, Saul S Value of Oscillometry in Study of Circulatory Disturbances of Extremities, *J. A. M. A.* **88** 1780 (June 4) 1927

38 Seneque, J *Presse med.* **35** 100 (April 9) 1927

coughed up by some of the experimental dogs as soon as the effect of the ether narcosis had diminished. The results of these experiments will be reported in a later paper.

#### COMMENT

The ability of the alveoli, bronchi and trachea to exscavenge themselves of infectious material seems to have received insufficient attention in the experimental studies in the production of abscess of the lung. How do the lungs keep their air passages clean? The bronchioles and alveoli end blindly, yet they are surprisingly clean. The stomach has hydrochloric acid which aids it to cope with bacteria that may enter it. No such chemical defense is known to exist in the lungs, however, bacteria do not manifest themselves readily in their air passages. Agglutinins, opsonins and other antibodies are not known to be present in the tissue of the lungs in unusual amounts.<sup>11</sup>

Three methods may serve to cleanse the air passages. The first, and perhaps the most effectual for large masses of foreign material, is the explosive expulsion of air and solid material during a cough. Even though there is little or no air in the alveoli beyond the foreign material, the elasticity of the surrounding air-containing lung is conducive to a squeezing out and an emptying of the nonair-containing portions during the act of coughing. The second factor in cleansing the air passages is the action of the ciliated epithelium. The ciliated epithelium may carry material to the pharynx, where it is unconsciously disposed of by swallowing. Undoubtedly, bacteria and pus may be expelled from the bronchi and trachea by the cilia lining them. A third factor in the removal of solid material from the lungs is the wandering cells of the blood stream.

In addition to these three methods of removal of foreign material from the air passages, the rôle played by posture may be mentioned. The use of iodized oil 40 per cent for diagnostic mapping of the bronchi demonstrates the facility of movement of fluids to the dependent portions of the air passages.

My co-workers and I do not wish to doubt the possibility that abscess of the lung may be due to the lodgment of infectious emboli in the radicals of the pulmonary arteries. We have produced such abscesses experimentally. We have, however, hoped to point out and to prove experimentally that the route of entry of the infectious material into the lungs may be through the air passages. A single infectious embolus, when entrapped in the pulmonary artery, may produce a single abscess of the lung, likewise, infectious material entrapped in the air passages

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<sup>11</sup> Kendall, I. A. Personal communication to the author.

# ARCHIVES OF SURGERY

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VOLUME 16

JANUARY, 1928—IN TWO PARTS—PART II

NUMBER 1

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## TRANSACTIONS OF THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

TENTH ANNUAL MEETING, NEW YORK CITY,  
MAY 9, 10 AND 11, 1927

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## CLINICAL STUDIES

Eighty-four consecutive cases of nontuberculous abscess of the lung constitute the basis of this study. Only the significant factors which seem to have relation to their etiology will be recorded here.

Briefly, nineteen, or 22 per cent, of these eighty-four cases of abscess of the lung followed tonsillectomy. The onset of symptoms varied in these cases from three to fourteen days after tonsillectomy. One case followed tonsillitis without tonsillectomy. Five cases, or 6 per cent, followed abdominal operations. On two of these patients an appendectomy was performed, on two a cholecystectomy and on one a gastroenterostomy. All of these patients were operated on under general anesthesia. One abscess of the lung followed mastoidectomy, one followed amputation of the leg and one followed resection of the tongue for carcinoma. The three last operations were also performed under general anesthesia. In all there were twenty-seven cases, or 32 per cent, the onset of which followed closely after an operative procedure. Each of these twenty-seven patients had had a general anesthetic with unusual opportunity for aspiration of infectious material. The onset of symptoms was delayed for several days, usually from six to eight days, after the operation and the administration of the anesthetic. Abscesses produced by experimental aspiration showed a similar latent period after injection of the infectious material into the bronchus.

In each of the patients on whom operative procedures had been performed preceding the development of the abscess of the lung, there was unusual opportunity for the occurrence of emboli as well as unusual opportunity for aspiration of infectious material. In forty-five, or 53 per cent, of these eighty-four patients, however, the onset of the symptoms did not follow emboli-producing procedures or conditions. The forty-five patients variously ascribed their abscesses to previous or concurrent infections of the respiratory tract, including "bronchitis," "exposure and took a cold," "pneumonia," "pleurisy," "flu" and "typhoid pneumonia." It is probable that many of the diagnoses were erroneous, and that the symptoms which led to the diagnoses were only the symptoms attendant on the development of the abscess in the lung. The abscesses in these cases (53 per cent) seem clearly to have been the result of an infection which reached the lung through the air passages, since there had not been an opportunity for the production of infectious emboli. Clinically, they did not differ from the abscesses which followed operative procedures. They usually had the similar foul odor, and there were multiple abscesses frequently confined to a single lobe of the lung. In these respects, they resembled experimental aspiratory abscesses.

# EXTRAPLEURAL RESECTION OF THE ESOPHAGUS

USE OF THE SAME INCISION AS THAT EMPLOYED  
IN MY TRANSPLEURAL METHOD

FRANZ TOREK, M D

NEW YORK

In resecting the esophagus for carcinoma, a thorough exposure of the esophagus is necessary as it is not sufficient to expose merely the new growth. The resection, in order to be radical, must include a good portion of the apparently uninvolved esophagus on either end of the tumor, and more room is needed to care properly for each divided end. If my method of drawing the upper stump out through the neck and invaginating the lower stump is employed—and that method is favored by many at present—much more room is needed. The required space is amply supplied in my method of transpleural approach through the whole length of the seventh intercostal space, augmented by the division of the four ribs above that space, near the spinal column.

It is universally agreed that the method referred to affords the necessary exposure and access. There are, however, differences of opinion as to the selection of a transpleural or an extrapleural approach. The advocates of the extrapleural method claim that the opening of the pleura entails certain dangers that could be avoided if the pleura were not opened, which is true. It occurred to me that it might be possible to combine the satisfactory exposure afforded by my transpleural method of approach with the advantages of an extrapleural operation as this combination is feasible. It takes somewhat longer than the transpleural method, and it remains to be seen whether the advantages of the extrapleural attack outweigh the loss of time.

## TECHNIC

The skin incision goes through the whole length of the seventh left intercostal space and continues from the posterior end of this incision upward to the third rib. It is then deepened through the muscles. In cutting down on the seventh interspace, great caution should be exercised when the intercostal muscles are reached, and this caution should be heightened to an extreme degree on dividing the internal intercostal muscle, so that the pleura may remain intact. This part of the operation, therefore, does not permit haste, the knife is to be handled lightly, and the incisions should be shallow. When the pleura has been well exposed in the seventh intercostal space, I begin to separate it from the thoracic wall. The initial steps of the separation are the most difficult. One may start with a blunt instrument like Kocher's gutter dissector, as soon as a little headway

# UNRESOLVED PNEUMONIA

A SURGICAL ANALYSIS \*

OTTO C PICKHARDT, M D

NEW YORK

Certain old medical terms that are all inclusive have been handed down from generation to generation. They are not terms for actual diagnoses under more modern methods of investigation, but are generalizations. Indigestion, rheumatism and other conditions come in this class, and I feel that the term "unresolved pneumonia" could be included in a large majority of cases. While undoubtedly there is such a condition, it is comparatively rare, and the diagnosis of unresolved pneumonia is usually a confession of failure to make a correct one. One has only to view its numerous synonyms commonly used to see how loosely the same condition is variously labeled. Among these may be mentioned interstitial pneumonia, chronic fibrous pneumonia, organizing pneumonia, protracted pneumonia, persistent pneumonia delayed resolution and, finally, basal fibrosis. The first three have a distinct pathologic picture which has often been described, and there can be no objection to them when correctly applied. Unfortunately, this is rarely the case.

MacCallum<sup>1</sup> stated

Occasionally, while the symptoms of the acute illness (pneumonia) disappear completely and the convalescence seems complete, a form of consolidation of the lung persists and is found to be due to a replacement of the exudate by fibrous tissue (fig 1).

Rohdenburg described the microscopic picture as follows

The lung alveoli are more or less completely filled with a meshwork of fibrin in which are entangled round and plasm cells. These wandering cells in many areas are transformed into connective tissue cells and slowly the alveolus instead of being an open space bounded by a lining of endothelium is changed to a mass of more or less dense connective tissue surrounded by endothelium.

Pneumonia, either lobar or lobular, is an acute disease, and the concept of its becoming a chronic condition in itself is rather difficult to understand. It seems more reasonable that there are, or may be, other contributing factors which will make it chronic. A new formation of fibrous tissue occurs, so that the lung becomes indurated, leathery and

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\* From the Department of Surgery, Lenox Hill Hospital

1 MacCallum, W G. Text-Book of Pathology, Philadelphia, W B Saunders Company, 1921, p 544

liberation of the entire esophagus, its division below the tumor, invagination of the lower stump, extraction of the esophagus through an incision in the neck and its transplantation into a subcutaneous antethoracic channel. The method of closure, likewise, is identical with that employed in the transpleural operation.



Fig 1—Roentgenographic appearance of the site of the carcinoma of the esophagus

#### APPLICATION OF METHOD

Thus far, I have not had a favorable case. In fact, I have completed the operation in only one case (fig 1), the others being merely explorations, as the tumors, after exposure, proved to be inoperable. In the case in which I performed the operation and in which the patient died on the fourth day, the tumor was situated behind the aortic arch, extending both above and below it. To release it some thoracic

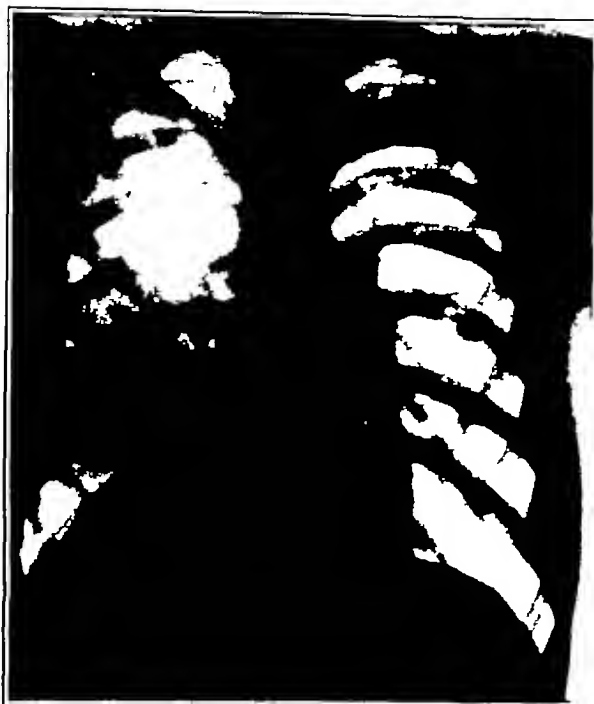


Fig 2 (case 1, table 3) —Unresolved pneumonia in the lower lobe of the right lung twenty-three days after onset

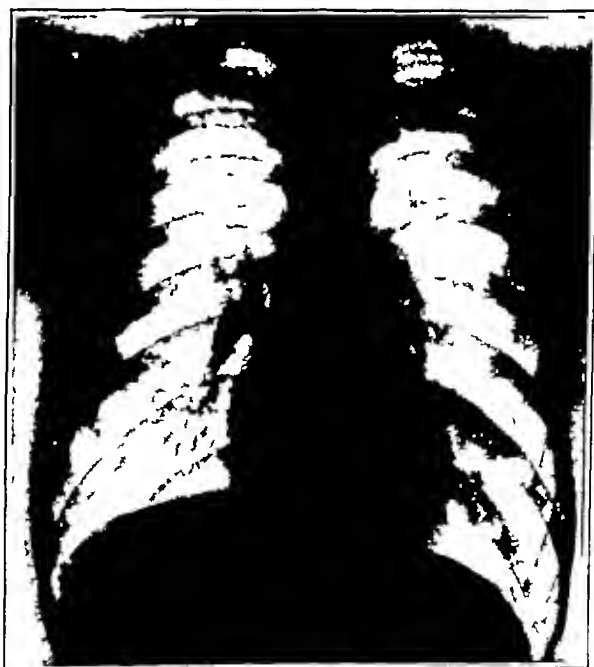


Fig 3—Same case as in figure 2 six years and three months later showing chronic peribronchial infiltration in the same area

An interesting fact connected with this case is the observation, with the aid of roentgenograms taken on the second day after operation, that there was no exudate in the pleura on the left side, the side on which the operation had been performed, but that the right side presented a haze with the evidence of an effusion (fig 2). The extensive handling of the left pleura from its outer side, without opening it did not disturb the normal transparency in the lung picture, whereas on the right side, which was simply opened but not otherwise handled, the haze of a beginning exudate appeared.

At autopsy the left pleural cavity was found to be free from adhesions and contained neither blood nor any other exudate. The pleura was tightly adherent at its parietal attachment to the ribs. The right pleural cavity contained about 500 cc of blood-stained serum. There was some fresh fibrin on the surface of the right lung. The left lung showed slight edema. Metastases were found at the junction of the esophagus and cardia in the shape of several islands of white, firm tissue, and at the upper edge of the pancreas as a circumscribed pinkish nodule, 2 cm in diameter, the microscopic diagnosis at both places being secondary squamous cell carcinoma. The primary tumor was a squamous cell epithelioma of the esophagus, 8 cm in length, showing a complete annular involvement. The lumen was completely obstructed for 5 cm.

Two months elapsed between gastrostomy and operation in this case, owing to the fact that the patient insisted on going home after the gastrostomy. The metastases helped to lower his resistance. While it is possible that they may have been overlooked at the time of the gastrostomy, in spite of careful search, they may also have arisen during the long delay between operations.

Those who have looked with favor on the advantages of the complete exposure afforded by my method of transpleural resection of the esophagus, but who, at the same time, would prefer to proceed by an extrapleural route, may perhaps be sufficiently interested in this method of extrapleural approach to give it an extended trial.

reaction which does not subside in normal fashion, and which is therefore erroneously labeled unresolved pneumonia

In 1913, Thacher<sup>3</sup> read a paper on this diagnosis and made an interesting report. He set a time limit of seventeen days during which a condition could rightly be called unresolved pneumonia. He analyzed thirty-four cases as follows: fourteen simple, mild trailer cases ending in recovery, six cases with miscellaneous complications, nine cases complicated by empyema, two cases complicated by abscess of the lung and three cases of probably simple delayed resolution. He stated

All patients, who, after pneumonia, are quite ill with a prolongation of fever, more are suffering from the presence of pus in the pleura or the lung, than from any other abnormal condition



Fig. 6—Same case as in figure 4 sixteen months later showing the peribronchial thickening in the lower lobe of the left lung

The examining physician should therefore keep in mind the pathologic differences between a real organizing pneumonia and the clinically similar but pathologically different picture presented by a patient in whom consolidation persists after pneumonia.

It is my purpose in this analysis, first, to present the many different types of lesions, both pulmonary and miscellaneous, which were actually found on closer investigation, and secondly, to show that in the rare positive case (six out of fifty-two), a definite type of lesion is found by means of the follow-up roentgenograms taken from sixteen months to

3 Thacher, J. S. Unresolved Pneumonia, *M. Rec.*, January, 1914

the feet 4 Throughout the operation ether is given in amounts sufficient to keep the patient quiet, but never to the point of an abolition of the swallowing reflex 5 The assistant is required to operate the suction tube and to keep the pharynx absolutely clear of mucus and blood 6 All bleeding vessels are ligated, and the operation usually requires the administration of ether for from thirty to forty-five minutes It is to these precautions, and particularly to the light anesthesia, that we ascribe the absence of postoperative infection of the lung in our cases If infected emboli are the cause of abscesses of the lung after tonsillectomy, it seems likely that this complication should have occurred in our cases with the same frequency that it has in some other clinics

In 1924, we began the study of experimentally produced abscess of the lung in dogs for the following purposes 1 To produce a chronic suppuration of the lung that was limited to one lobe and not complicated by pneumonia or empyema 2 To compare the blood pressure in the pulmonary artery in normal dogs with that in animals with a chronic suppuration of the lung 3 To determine the effect on the heart of ligation of the pulmonary artery and vein to one lobe in normal dogs, and to compare it with that observed in animals with a chronic abscess of the lung 4 To try various methods of removing the infected lobe and closing the bronchial stump The first two years of this investigation were occupied by the attempt to produce a chronic abscess of the lung During the past year, we have attained our first objective, but we have not yet carried out the remainder of the program By introducing through a bronchoscope a small piece of cotton saturated with fresh scrapings from pyorrhea cavities in patients, we finally succeeded in producing a chronic lung abscess that remained localized to one lobe and was not associated with a general pneumonitis These pyorrhea scrapings were swarming with spirochetes and other bacteria, but we have made no attempt as yet to isolate the organisms and to determine whether any one type was chiefly responsible for the infection in the lung In eight animals, an abscess of the lung with cavity formation and necrosis of an entire lobe was produced by direct inoculation of the main bronchus of the lobe through a bronchoscope Abscess of the lung developed in a lower lobe of two additional animals, after introduction into the frontal sinus of a piece of cotton soaked with fresh scrapings from a pyorrhea cavity in a patient Bronchoscopy was not performed on these two animals The frontal sinus was opened through an external incision, the infected pledget of cotton was placed in the cavity through a small burr opening, and the wound was closed Both of these animals developed a suppuration in the frontal sinus with the constant discharge of foul-smelling pus from the nostril, and both died from pulmonary hemorrhage after six weeks The hemorrhage was due to the erosion of a large blood vessel in the abscess cavity This experiment indicates that



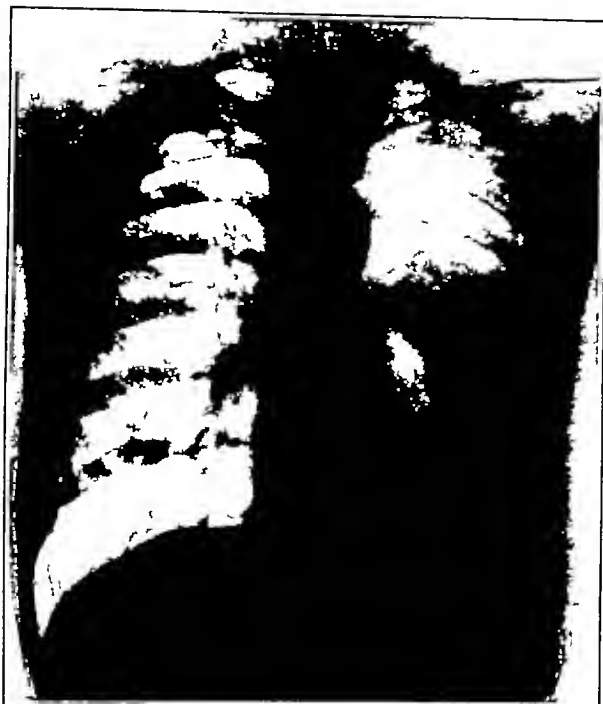


Figure 9

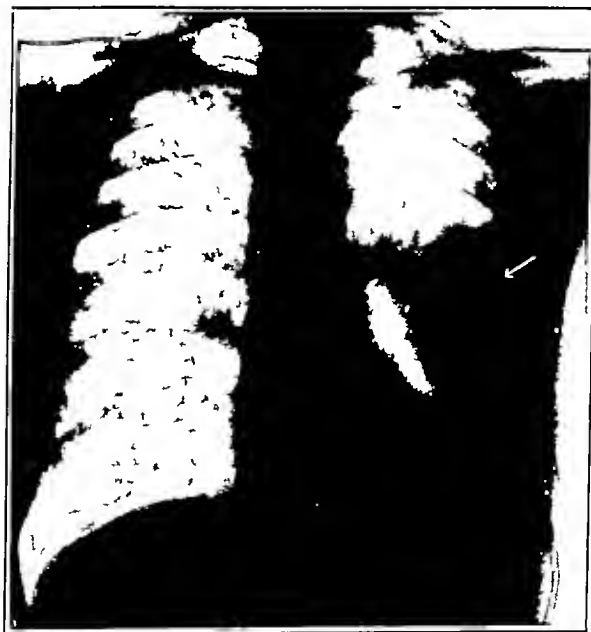


Figure 10

# ETIOLOGY OF ABSCESS OF THE LUNG

## EXPERIMENTAL AND CLINICAL STUDIES \*

DUFF S ALLEN, MD  
ST LOUIS

The causative factors of nontuberculous abscesses of the lung are not fully known. How does the infection reach the lungs? Are there specific bacteria? Why does one person develop an abscess of the lung after a certain operative procedure while another person does not acquire such an abscess after an apparently identical procedure? This is a report of the experimental production of abscesses of the lung by aspiration, and the translation of these experimental observations into some of their clinical correlatives.

### ROUTES OF ENTRY

There are three possible routes of entry for the infection in abscess of the lung. The first is direct, by way of the respiratory passages; the second is indirect, by way of the blood stream, and the third is by way of the lymphatics. The direct aspiratory route and the indirect route through the blood stream have seemed the most probable routes of entry.

A considerable percentage of abscesses of the lung follow operative procedures within the mouth, nose or throat. For these, at least, the question of whether the chief route of entry for the infection is through the blood stream or whether it lies through the respiratory passages is of the utmost importance.

If the infection reaches the lungs through the air passages, then the incidence of abscess of the lung following tonsillectomy or other operations about the upper respiratory tract and mouth might be lowered materially by the avoidance of aspiration of infectious material at these operations. If, on the contrary, the infection reaches the lungs through the blood stream as infectious emboli and not by aspiration, then the amount of aspirated blood or other infectious material that may be sucked into the lungs during these operations is of little consequence for postoperative abscess of the lung.

If the embolic route is the principal route of entry, the surgeon should direct his attention toward the prevention of dislodgment of infectious emboli. If the aspiratory route is the chief route of entry, the surgeon should prevent aspiration of infectious material. Furthermore, the spontaneous development of nontuberculous abscess of the lung might be avoided by proper attention to oral hygiene and hygiene of the upper respiratory tract and to pathologic processes in these areas.

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\*From the Department of Surgery, Washington University School of Medicine and Barnes Hospital, St. Louis.

four years later. This lesion may be expressed as being a peribronchial infiltration and thickening due to increase in the connective tissue, localized in the formerly consolidated area. The picture is similar to that seen in a chronic bronchitis, except that in the latter the condition is found generalized throughout the whole bronchial tree (cases 1, 10, 44, 48, 52, table 3).

In order to get at a definite basis, it was decided to go through the request slips for roentgen-ray examination of the Lenox Hill Hospital and to pick out those on which had been written "unresolved pneumonia." Between January, 1922, and December, 1926, there were 2,773 requests for roentgen-ray examination of the chest for twenty-one different pulmonary and bronchial conditions, conditions of the heart were excluded



Figure 13

Of these, 591 mentioned the word pneumonia and forty-one "unresolved pneumonia." In addition, eleven cases were added through personal communications. It is to be remembered that the staff at the Lenox Hill Hospital has been among the pioneers in employing surgical procedures for conditions of the lung, and many cases of undiagnosed conditions of the lung have been received for study. Many of these patients are sent to the hospital with the diagnosis of "unresolved pneumonia," and therefore are sent to the roentgen-ray department.

In this series, cases are not considered in which the normal pneumonic crisis or normal resolution has not had time to occur, say up to the ninth day, and which have erroneously, merely from a standpoint of time, been designated unresolved pneumonia. In a general review of other cases reported in the literature, I did not find any definite time limit in which a case of pneumonia became unresolved. Frequently

succeeded in producing acute abscesses with formation of a cavity by the introduction of a single embolus into the pulmonary circulation. They failed to produce aspiratory abscess of the lung, and, therefore, concluded that most abscesses of the lung in the human being were embolic rather than aspiratory in origin. They consider this to be especially true in those cases of abscess of the lung that follow operative procedures. They agree with Fetterolf and Fox,<sup>12</sup> who believe that most abscesses of the lung following tonsillectomies are due to emboli dislodged from the paratonsillar tissues.

#### EXPERIMENTS

Acute nontuberculous abscess of the lung was produced in dogs both by the liberation of emboli into the femoral vein and by the intrabronchial injection of pus from chronic nontuberculous abscesses of the lung. For the sake of brevity, only the latter experiments, in which abscess of the lung was produced by the intrabronchial introduction of pus from subjects with abscess of the lung, will be reported here in detail. This group of aspiratory abscesses of the lung is a most important feature of this report.

**SERIES I**—Experiments in fifteen rats make up this series. Pus was obtained from cases of chronic, nontuberculous abscesses of the lung. The patients were requested to cough and expectorate the pus into a sterile cup over a period of several hours. The infectious material was then slowly introduced into the exposed trachea of the rat by the method suggested by Smith. Not a single rat developed an abscess of the lung or pneumonia.

The most probable explanation of the failure to produce infection in the lungs of these experimental animals seemed to be that the pus contained only avirulent bacteria, or perhaps that the "invasive" bacteria had been killed by chilling of the pus before it had been introduced into the trachea. Smears of the pus taken at the time of its injection showed the presence of many cocci, fusiform bacilli and spirochetes. The spirochetes found in the respiratory tract in normal persons are thermolabile. They are often killed by a fifteen minute exposure at room temperature. It seemed advisable to inject the warm pus into the bronchi of animals immediately after it had been coughed up from the lungs.

The following experiment illustrates the procedure followed in experimental series II.

**SERIES II**—*History*—B, a boy, aged 17, had had a bronchiectatic abscess of the lung for the past twelve years. As much as 200 cc of pus could be coughed up at one time when the patient instituted postural drainage by leaning over a chair. As the etherized dog could not be taken into the ward of the hospital, the patient was requested to come to the laboratory. On Feb 19, 1927 a small, healthy, active, young dog was anesthetized with ether. A soft, rubber catheter, size 10

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<sup>12</sup> Fetterolf, G, and Fox, H. The Reaction of the Para-Tonsillar Tissue to Tonsillectomy. A Study in the Etiology of Post-Tonsillectomy Pulmonary Abscess, *Am J M Sc* **166** 802, 1923

cases have been so designated in which the patients have not had time to become well either by crisis or by lysis. The average time between the onset and the tentative diagnosis in the cases here reported is fifty-five days, varying between fourteen days to one year.

One can readily understand how, except in a few cases, the diagnoses in table 1 were lumped into one grand group of "unresolved pneumonia," when one remembers that many of these patients lived where there were

TABLE 1—*Summary of Final Diagnoses*

Conditions	Number of Cases
Lobar pneumonia, bronchopneumonia, resolving or unresolved, but not finally checked up (see table 3)	10
Pleurisy, suppurative	7
Abscess of lung	5
Neoplasm, lungs	4
Bronchitis, acute and chronic	3
Pulmonary tuberculosis, chronic	3
Chronic pneumonia and pleurisy with effusion	2
Pleurisy with effusion	2
Pleurisy, serofibrinous	2
Tuberculous pneumonia, acute	2
Pulmonary tuberculosis and abscess of lung (pneumococcus)	1
Bronchiectasis	1
Neoplasm, pleura	1
Foreign body, bronchus	1
Pertussis	1
Mediastinal tumor, Hodgkin's disease	1
Abscess of liver	1
Subdiaphragmatic abscess	1
Anemia, pernicious	1
Arthritis, chronic, shoulder	1
Osteomyelitis, femur, acute	1
Pyelitis	1

TABLE 2—*Classification According to Types*

Conditions	Number of Cases	Percentage
Unresolved pneumonia	6	11.5
Pleurisy, suppurative	7	13.5
Abscess of lung	6	11.5
Pleurisy with effusion (various types)	6	11.5
Neoplasm, lungs and pleura	5	9.6
Pulmonary tuberculosis	5	9.6
Bronchial system	4	7.7
Foreign body	1	1.9
Miscellaneous	12	23.1
Frankly Surgical Conditions		
Types 2, 3, 5, 8	19	36.5

no hospital facilities for the taking of roentgenograms or the performing of a bronchoscopy.

If one adds together the cases of suppurative pleurisy, abscess of lung, neoplasm, and foreign body, one has a class of cases amounting to 36.5 per cent which at some stage of their development were frankly surgical conditions. This excludes pleurisy with effusion in which simple aspiration is usually sufficient and the various types of tuberculosis, many of which are now being successfully helped by operation.

Table 3 shows a more detailed analysis of all the cases which superficially were apparently unresolved pneumonia. On checking these up

This experiment of injecting warm, fresh pus from nontuberculous abscesses of the lung into the bronchus was repeated in seventeen dogs and three rabbits, making a total of twenty-one experiments in series II. Only three dogs developed abscesses of the lungs. The remaining fifteen dogs did not develop either abscess of the lungs or pneumonia. Roentgenograms were made and auscultation was performed repeatedly over a period of two months. The animals remained active and did not show signs of abscess. One rabbit developed pneumonia and died at the end of twenty-four hours. The remaining two rabbits lived and did not show signs of abscess at the end of fifty-two days.

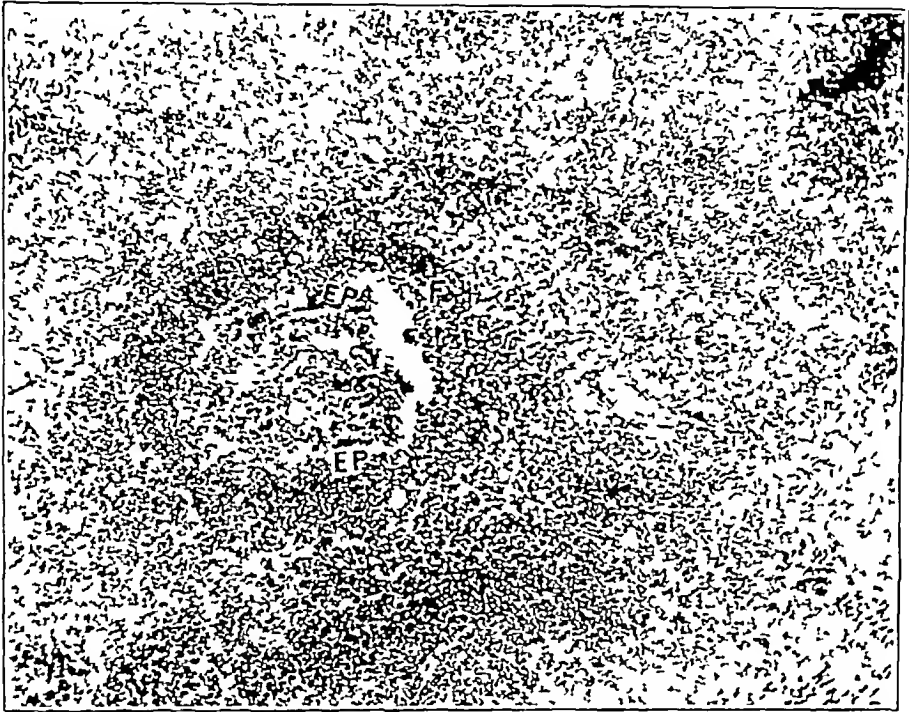


Fig 1—Erosion of epithelial lining of bronchiole due to infectious process. The fibrous tissue ring, *F*, of the wall is intact. Epithelial casts, *Ep*, can be seen clinging to the fibrous tissue. Bacteria were not found in the walls of the blood vessels or in their contents. Bacteria were seen throughout the wall of the bronchiole and the surrounding tissue.

The three dogs in which multiple abscesses of the lung developed after aspiration of pus from abscess of the lung are of special interest. For the sake of brevity, the two latter experiments will not be described in detail, as I have described the first. After intrabronchial injection of pus, the dogs all exhibited a latent period before the onset of malaise. None of the three animals was observed to cough though all of them had pus in the trachea and bronchi at necropsy. None of the three had an abscess with a cavity. The condition in the dogs therefore resembles the usual early abscess of the lung as it appears

carefully, I find that only six of ten can honestly be so classed, the other four must fall into the miscellaneous group. In this connection, it is interesting to note that whereas apparently definite signs of consolidation were found by physical examination of the lungs, the roentgenograms were negative for such a condition. According to this analysis of fifty-two cases, in only six, or 11.5 per cent, was the diagnosis of unresolved pneumonia correct. It seems as if the fallacy of this tentative diagnosis is being continued, and that therefore a more detailed and comprehensive study of this type of case is necessary before such a diagnosis can finally be made.

The internist can expect and should seek a more definite diagnosis in this class of usually undiagnosed pulmonary conditions by consultation with the bronchoscopist, the roentgenologist and the thoracic surgeon. The thoracic surgeon should be consulted with a view to curing by operation a large percentage of patients with a hitherto anomalous medical condition.

#### CONCLUSIONS

- 1 True primary unresolved pneumonia is rare.
- 2 In the rare positive case, a definite localized peribronchial infiltration, visible in the roentgenograms, develops later.
- 3 Approximately 36.5 per cent of pulmonary conditions diagnosed as unresolved pneumonia will be frankly surgical conditions.
- 4 The thoracic surgeon should be consulted more frequently when pneumonia does not resolve promptly and properly.

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Attempts were made to entrap bacteria in the alveoli and smaller bronchi. It seemed that the formation of an abscess or some other manifestation of an infectious process would inevitably follow the confining of bacteria in the smaller air passages. Slugs of infectious tonsil and small pieces of beef contaminated by virulent bacteria were blown into the bronchi with compressed air. Abscesses did not develop in seven experimental dogs. Autopsy invariably showed that these infectious materials had escaped from the bronchi. The great difficulty in keeping infectious material in the air passages was soon evident.

Warm pus obtained from a patient with a foul, chronic abscess of the lung was next injected into the bronchus leading to one lobe, after which this bronchus was immediately ligated with silk. The procedure is illustrated in the following experiment.

**SERIES III—History**—On April 2, 1927, under ether narcosis, artificial respiration was maintained by the Gesel-Erlanger intermittent positive pressure artificial respiration apparatus. The dog was placed on its left side. An intercostal incision was made between the fourth and fifth ribs in the right side of the chest. The bronchus to the middle lobe was exposed by isolation of its accompanying pulmonary artery and pulmonary vein. The middle lobe was carefully avoided in this procedure in order to prevent injury to its alveoli. A stout silk ligature was passed beneath the pulmonary artery and vein to the lobe and carefully carried around the bronchus to encircle it completely. A soft rubber catheter of small caliber (no. 10 French) was now passed into the trachea by an assistant, and when the end of the catheter was felt to enter the bronchus to the middle lobe of the right lung, 3 cc. of the warm pus was injected into the bronchus, and the ligature was immediately tightened as the catheter was withdrawn. The wall of the chest was then closed without drainage.

April 3. Some dyspnea was present, but the dog was active and ate.

April 5. The dog was active, and did not appear to be sick.

April 7. Swelling appeared about the thoracotomy wound. The dog frisked about the room when he was taken from the cage.

April 10. The dog was sick, hung his head and coughed (this was the only dog which coughed). *Foul pus dripped from the nostrils.*

April 11. The thoracotomy wound was open. When the dog coughed, air gushed from the wound, but did not seem to enter the chest through the wound. The dog appeared to have bronchial fistula.

April 15. The thoracotomy wound was closed. The animal still coughed, appeared listless and was losing weight.

April 21. The dog coughed. Chocolate colored, foul-smelling pus dripped from the nostrils.

April 25. The dog was more active, but had lost a great amount of weight. He coughed but did not expectorate pus.

April 28. The dog was weak and emaciated. He was fairly active and did not have pain. To avoid the possibility of suffering due to extreme emaciation the dog was killed.

**Autopsy**—The thoracotomy wound was closed with granulation tissue. The left side of the chest did not contain fluid or pus. The left lung appeared normal. The mediastinal lobe was lying free in its mediastinal pocket on the pleura.



# NONTUBERCULOUS PULMONARY SUPPURATION

## A COMPARISON OF OPERATIONS AND THEIR RESULTS

HOWARD LILIENTHAL, M D

NEW YORK

The scientific selection of operative therapy in pulmonary suppuration is still in a state of development. Standardization is often a poor principle when applied to any phase of surgical work except the technic, and possibly even here it is particularly out of place in dealing with conditions the pathologic anatomy and biologic status of which show such fine distinctions as do those encountered in suppurative infections of the lungs. The frequent complication by disease of other structures, particularly of the pleura, adds still another problem to this perplexing question.

I need not discuss an exact classification of the various types of suppuration, although the blood-borne and the air-borne sources—the one beginning in the parenchyma of the lung and the other beginning in the bronchial tree and its ramifications—may roughly be recognized. To these may be added infection from contiguous structures. When changes related to the stage of the process and the organism which produces the infection are also recognized, one finds that confusion ensues. Going farther, varied anatomic characteristics in different portions of the same diseased organ are encountered. It must also be realized that in the lung one form of suppurative disease almost invariably produces another, such as abscess developing from bronchiectasis.

Few, if any, surgeons have had sufficient experience with all of the methods of operating in these diseases to confer authority. One operator may have been fortunate in the immediate results of bronchostomy, another may be satisfied with destruction by cautery, still another may have faith in some form of compression, and so on. Until one procedure has been used in many hundreds of cases of approximately the same condition, improvement in the methods of operation will be made slowly. All those who have had experience should record their results, for with the accumulation of evidence, the right technic may finally be approached. This is the reason why I present the conclusions which I have reached from my own clinical work.

The material examined consists of 105 unselected patients who were referred to me for operation and in whom lobectomy was neither performed nor contemplated. The list of conditions includes most of the forms of surgical pulmonary suppurative disease with the exception of tuberculosis and actinomycosis. I have also excluded the military cases and those of civilian traumatic surgery.

lobe They were identical in appearance to the spirochetes found in the tonsil which had been insufflated into and trapped in the bronchus

The experiment was repeated with a mixture of virulent streptococcus, staphylococcus, colon bacillus and pyocyanus The animal died on the fourth day of pneumonia of the right upper middle and lower lobes and beginning empyema of the right pleural cavity

Four control experiments in dogs in which the bronchus to the middle right lobe was ligated without the intentional introduction of infectious material into the bronchus failed to develop abscess This, and the fact that following the aspiration of pus-containing fusiform bacilli and spirochetes, the abscesses of the lung in animals with liga-

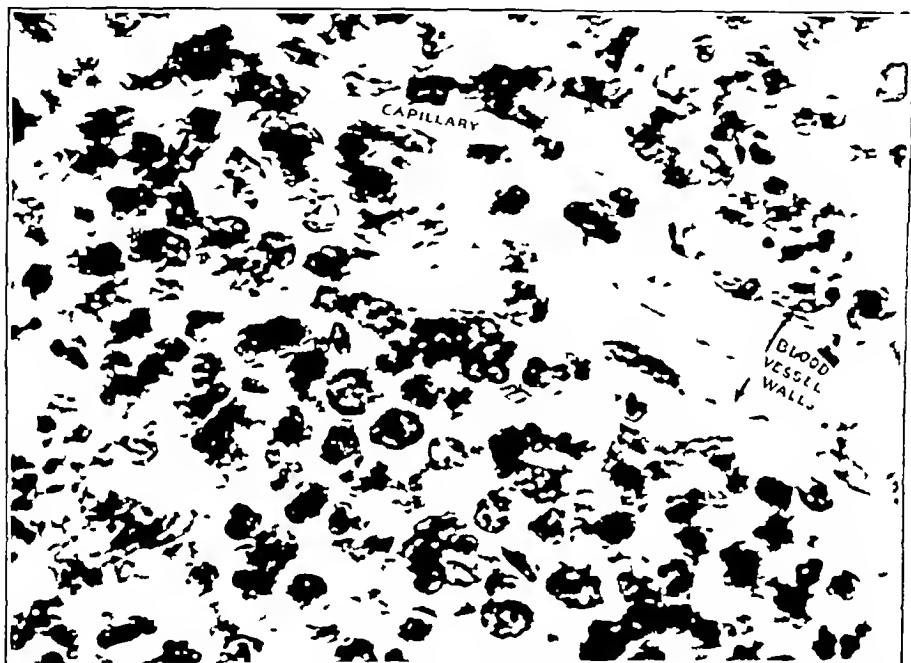


Fig 3—Intact capillaries in an aspiratory abscess The stained section showed the capillaries filled with intact red blood cells

ture of the bronchus contained identical bacteria seemed to show that blocking of the respiratory passages was an important factor in the production of these abscesses

Less complicated methods than ligation of the bronchus to a lobe to produce obstruction are being tried Siebert<sup>13</sup> had produced this blockage by the use of talcum powder before the latter series of experiments was begun More recently, I introduced contaminated millet heads with the barbs pointing toward the larva This was accomplished through a bronchoscope, the millet head being placed in the smaller bronchus under the control of vision Even these grass heads were

13 Siebert W Personal communication to the author

Table 1 represents the causes of the pulmonary infections as far as I was able to assign them

In a number of cases, intranasal infection from various causes was present and sometimes was etiologic. The nose should always be examined, especially when a radical operation on the lung is planned.

There was a total of forty-seven deaths, or 45 per cent, and of these, sixteen may fairly be ascribed to septic conditions which existed before operation. By this I mean that these sixteen patients would probably have died of their disease if they had been treated medically.

In nine cases, postoperative cerebral embolic conditions were directly responsible for death. Three of these deaths were due to air embolism and the remaining six to bacterial infection. Nine patients died of

TABLE 1—*Causes of Pulmonary Infection*

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Congenital	4
Chronic bronchiectasis	2
Pneumonia, including influenza, etc	29
Syphilis	1
Diverticulum of esophagus	1
Cardiospasm	1
Puncture of the esophagus from within	1
Aspiration pneumonia not following operation	3
Nasal operation	1
Tooth extraction	1
Fracture of thigh	1
Osteomyelitis of ribs	1
Confinement	1
Cholecystectomy	1
Appendectomy	5
Tonsillectomy	21
Hemorrhoidectomy	1
Direct extension from abdomen	1
Unknown	29
	<hr/>
	105

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hemorrhage either from the wound or from the mouth or from both. There was one fatal mediastinitis. Two patients died from phlegmon of the wall of the chest produced by diagnostic puncture of abscess of the lung. Seven died of contralateral pulmonary conditions, including pneumonia, edema and abscess. In the cases of abscess, it was not always possible to differentiate between preoperative and postoperative conditions. Two patients died from shock and one from acute nephritis not present before operation.

These causes of death will be briefly discussed in order.

*Cerebral Conditions*—(a) *Air Embolism*. It is understood that this accident may result from the entrance of air into even a small branch of the pulmonary return system. As air is lighter than blood, it is manifest that the erect posture during operations or other manipulations on indurated tissue within the chest is dangerous. It is good practice, therefore, to operate in these cases with the head of the patient lower than the thorax. Air embolism from the lung is rare except as an operative accident.

may produce multiple abscesses of the lung. The principal requisite in either case is that the infectious material is not allowed to escape from the lung.

The fact that in the five experimental aspiratory abscesses of dogs each involved lobe had multiple abscesses is of the greatest clinical significance. Most patients with abscess of the lung exhibit multiple abscesses rather than a single abscess with a cavity. During the operation of cauterized pneumectomy, as advocated by Graham,<sup>15</sup> great numbers of smaller abscesses are usually encountered in the infected area of the lobe.

That experimental abscess of the lung may be produced by the lodgment of infectious emboli has been repeatedly shown. Cutler and Holman, Weidlein and Schlueter<sup>10</sup> devised a uniformly successful and ingenious method for producing such embolic abscesses by using a

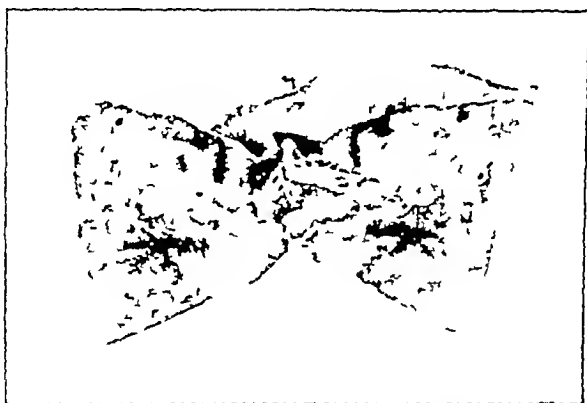


Fig. 4—Cut surface of a lobe of lung containing multiple aspiratory abscesses. Note the bronchioles in the central portions of the abscesses.

segment of vein containing various kinds of bacteria. Cutler and Schlueter<sup>9</sup> and Schlueter and Weidlein<sup>11</sup> reported a large series of experimental abscesses of the lung produced in this manner. They hold that abscesses of the lung following operations have an etiology different from those abscesses which do not follow operations. Smith<sup>1</sup> doubted this. He compiled reports of fifty-six cases from the literature in which bacteriologic and pathologic studies had been made and he did not find any difference in these respects between abscesses of the lung following operations and those in which operation had not preceded the onset of the abscess. We cannot determine whether the abscess has followed an operative procedure or not, except by questioning of the patient.

Experimental results indicate the possibility that the infection may reach the lung through the air passages in clinical abscess of the lung.

<sup>15</sup> Graham, E. A. Pneumectomy with the Cautery. *J. A. M. A.* 81:1010 (Sept. 22) 1923.

## RECOVERIES AND DEATHS

In table 2 three cases are included in which the cautery was used in the lung. In two of these, a considerable portion of tissue was destroyed. One death resulted from hemorrhage at the wound and by mouth, and one from a cerebral metastasis. In the remaining case, death followed the destruction of part of a wall of the abscess for the purpose

TABLE 2—*Percentage of Deaths and Number of Recoveries from Different Procedures, Including Clinical Cures*

Condition	Cases	Recoveries	Deaths	Percentage
Artificial pneumothorax	2	2	0	0
Thoracoplasty	13	4	5	33
Pneumonolysis extrapleural	5	2	2	40
Pneumonolysis intrapleural	2	0	2	100
Drainage	57	30	18	32
Pneumonotomy	15	3	11	73
Bronchostomy	15	7	5	33
Diagnostic puncture of abscess	3	1	2	67
Preliminary thoracotomy	2	0	2	100

of drainage. A severe hemorrhage at the wound and by mouth, during a dressing, could not be checked by packing.

My unfortunate experience with the cautery should be compared with the many excellent results reported by Graham. One cannot help being influenced by his earlier cases, but I would not attempt to deter others from using the soldering iron, perhaps I shall have better results in the future.

These figures are given for what they are worth. It would be impossible in a paper of this kind, and perhaps even in any event, to show statistically other results than those which come under the classification

TABLE 3—*Age Incidence*

Age Decades	Cases	Deaths	Percentage
1 to 10	10	3	30
10 to 20	11	4	36
20 to 30	26	12	42
30 to 40	20	6	30
40 to 50	22	12	55
50 to 65	16	10	63

of "well," "clinical cure" or "death." I shall, therefore, not attempt to record them otherwise than under the headings of "deaths" and "recoveries," including "well" and "clinical cure" under "recovery." By clinical cure, I mean that the patient was able to work and was satisfied with his condition.

Age as a factor is represented in table 3.

The danger of increasing age is, therefore, represented as follows. In patients up to 50, the mortality was 42 per cent, while from 50 to 65 it was 63 per cent—a matter of interest principally with regard to prognosis.

The remaining eleven abscesses of the lungs in this series of eighty-four were distributed as single instances, the onset of which followed respectively, aspiration of bone from a pork chop fracture of rib craniotomy, carcinoma of the esophagus, postpartum metritis, severe trauma with fracture of the leg, paranephritic abscess (?), empyema in which a rubber tube had been lost after thoracostomy, empyema and infection of a tooth, one was a primary carcinoma of the lung with abscess. Conclusions should not be drawn from these isolated instances of abscesses of the lung.

There can be but little doubt that much infectious material reaches the smaller air passages, not only during operative procedures about the upper respiratory tract, but during general anesthesia and in ordinary breathing. Myerson<sup>16</sup> examined the trachea and larger bronchi in 100 cases following tonsillectomy. Blood was present in seventy-nine instances. Lemon<sup>17</sup> found that in dogs under ether narcosis, materials which had been placed in the mouth could be recovered from the smaller air passages. The intrapharyngeal instillation of iodized oil into the trachea, first successfully used by Singer<sup>18</sup> illustrates the ease with which the contents of the pharynx may reach the lungs during ordinary inspiration. Why, then, is not abscess of the lung a more common disease?

The experiments have shown the ease by which infectious material escapes from the bronchi and trachea. In addition I should like to point out the fact that the air passages are normally lined with an unbroken epithelium. They are, in reality, a part of the "exterior" of the body. The experiments show that the lining epithelium may be destroyed by certain bacteria confined within the smaller air passages. Abscesses are then formed within the lung.

#### CONCLUSION

1 Multiple abscess of the lung may be produced in dogs by the injection into the bronchus of warm pus from patients with chronic abscess of the lung. The dogs, in the experiments described were under ether narcosis at the time of contamination of the bronchus.

2 Clinical abscesses of the lung are usually multiple and are often confined to one lobe.

3 Obstruction of the bronchus plays a dominant role in the formation of experimental aspiratory abscess of the lung.

16 Myerson, M. C. Pulmonary Aspects of Tonsillectomy under General Anesthesia, *Laryngoscope* **32** 929, 1922.

17 Lemon, W. S. Aspiration. Experimental Study. *Arch. Surg.* **12** 187 (Jan.) 1926.

18 Singer, J. J. Bronchography. *Arch. Surg.* **14** 167 (Jan.) 1927.

interstitial, true general drainage is almost impossible, but after incision, I have seen the indurated tissue break down and slough away

*Bronchostomy*—Bronchostomy is often followed by surprisingly good immediate results, but the patient's ultimate condition cannot be considered ideal. The dangers of slowly spreading gangrene with recurrent hemorrhages even years after the establishment of the stoma give a sense of insecurity to the surgeon who has encountered these late accidents

*Diagnostic Puncture of Abscess*—The performance of puncture for the purpose of diagnosis need be mentioned only to condemn it. I have observed many fatal cases in addition to those mentioned in my table and in which extensive operation for the ensuing phlegmon has been unavailing. A cure rarely results from drainage of the phlegmon and of the abscess of the lung

#### COMMENT

When one reviews the material which forms the basis of this presentation one is struck by the high mortality rate of 45 per cent in operative cases. In glancing over a paper by MacKenzie<sup>2</sup> I note that he gives the mortality rate as from 40 per cent to 80 per cent, although in 169 cases from Bellevue Hospital, the death rate was about 40 per cent. He does not make any distinction between the cases in which operation was performed and those in which it was not performed. In the same paper this strong statement is found: "When a lung abscess does not terminate fatally or in spontaneous cure, there ensues a condition of invalidism to which death itself seems preferable." The type of patients to which he refers will probably finally die either of some condition directly connected with the abscess of the lung or of the consequent chronic sepsis with or without amyloid disease. It is difficult to calculate statistics in these circumstances.

My paper has been written in order to call attention to this aspect of suppuration of the lung. If recovery is not complete, whether or not operation has been performed, the probability is that the patient will finally succumb to his disease or to its sequelae. The cases must be followed for years if one is to get at the truth and not be satisfied with mere impressions. If palliative measures alone are used, the final mortality rate will be high—approximating MacKenzie's 80 per cent, or even more. One must not be deceived by the discharge of a living patient from the hospital. Incomplete operations, on the other hand, may be expedient, though undesirable, and it is the function of the thoracic surgeon to prolong comfortable existence even though he does not lose sight of the ever present danger.

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<sup>2</sup> MacKenzie, L. B. M. J. & Record **119** 191 (Feb) 1924

dry, analogous to that condition which appears in other organs, such as the kidney and the liver in chronic congestion. But this process requires time, and a constant focus of infection, a nidus of pneumococci or other bacteria, or some irritant must continue to be present, then it can readily be seen that the pathologic changes occur as a protective measure. This new fibrous tissue may occur by a slow hyperplasia of the existing fibrous tissue or by the formation of granulation tissue which gradually becomes denser with contraction. When an acute infection has either refused to subside normally or has caused apparently temporary pathologic changes which persist, with a rise in temperature and other signs, a surgeon naturally thinks that the causative agent is still present either in smaller

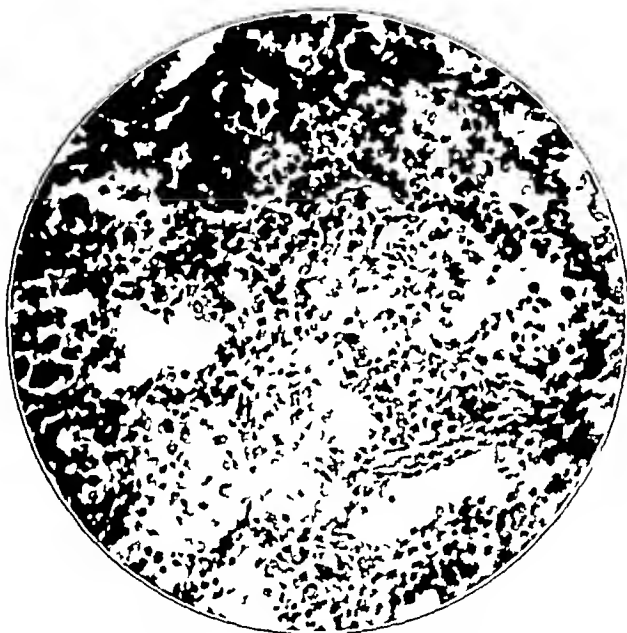


Fig. 1—Unresolved pneumonia

numbers or in an attenuated form. In other words, in the condition under discussion, a residual focus frequently remains which often forms pus either within the lung tissue or extrapleurally.

Piersoll<sup>2</sup> stated that there are two main classes of cases that are diagnosed as unresolved pneumonia: (1) true unresolved pneumonia and (2) pneumonic sequelae. I would add a third class, 'pneumonic precursors or forerunners.' In the latter class, some other primary condition is the underlying cause of the pneumonia itself, as, for instance, tuberculosis, tumor of the lung, a foreign body, bronchiectatic cavities, syphilis and other conditions. The cases in this class are more numerous than is usually thought, frequently there is a long drawn out inflammatory

2 Piersoll J. M. Unresolved Pneumonia. Penn. M. J. 25: 249, 1922.



favorably with that following much smaller operative procedures on the lungs and pleura. Granted that the early postoperative mortality is high, say 45 per cent, when only one lobe is removed, this must be balanced against mere palliation or even the so-called clinical cures of permanent bronchostomy with their chances for late fatal complications.

The more I study this question, the more I am inclined to favor lobectomy in appropriate circumstances. In the category of cases suitable for the performance of an operation, I would include only those in which the patient is under 35 years of age, and in which the blood pressure is more than 120 and the patient's general physical resistance apparently is high.

When I performed lobectomies in the earlier part of my thoracic work, I naturally chose the worst surgical risks. The mortality rate in my cases after the performance of this operation at that time was about 40 per cent when a single lobe was extirpated, and I am certain, from my experience with operations not so complete, that the statistics of ultimate cures would be on the side of the radical procedure. One is too apt to regard the mere discharge of a patient from the hospital, although he is still expectorating and usually has a permanent opening in the thorax, as representing a cure. When there is a bronchiectatic suppuration in more than one lobe, or when complications arise from previous operations, such as a dense mass of intrathoracic adhesions, lobectomy is out of the question, and one must be satisfied with far less than an ideal recovery.

#### SUMMARY

- 1 The number of cases presented is 105, all of which were operative.
  - 2 Lobectomy was not performed or contemplated in any case in these series.
  - 3 Tables represent operative and other statistics.
  - 4 A brief comparison of these operations with lobectomy leads to the recommendation that the radical procedure should be preferred in suitable instances.
- 52 East Eighty-Second Street



Fig 4 (case 44, table 3) —Unresolved pneumonia in the lower lobe of the left lung sixty-three days after onset



Fig 5—Same case as in figure 4 fourteen days later The consolidation has cleared up

for two years, one in which a little cross-bar pin was present for thirteen years and one in which a tack was retained for twenty-three years

Of the four cases in which the foreign body could be removed, i. e., the piece of wood, the tack, the pig knuckle and the cross-bar pin, recovery occurred in three. In one, suppuration persisted, and a lobectomy was performed, the patient died while he was being taken off the table



Fig 1—Abscess of the lung three weeks after operation in a child, aged 2 years

Sixty-eight of the 103 patients were treated by bronchoscopy. Before considering treating a patient with abscess of the lung by bronchoscopy, I arbitrarily set the number of bronchoscopies as three. It usually required two bronchoscopies to get acquainted with the patient. Patients are frightened the first time, and one can only pass the tube in and out, the second time, when they are not so frightened, one can learn something, the third time, one can get results. Three



Figs 7 to 13 (case 48, table 3) —Gradual clearing up of an unresolved pneumonia through a period of ninety-seven days. A final follow-up (roentgenogram not shown here) again shows peribronchial thickening.



Figure 8





Figure 11

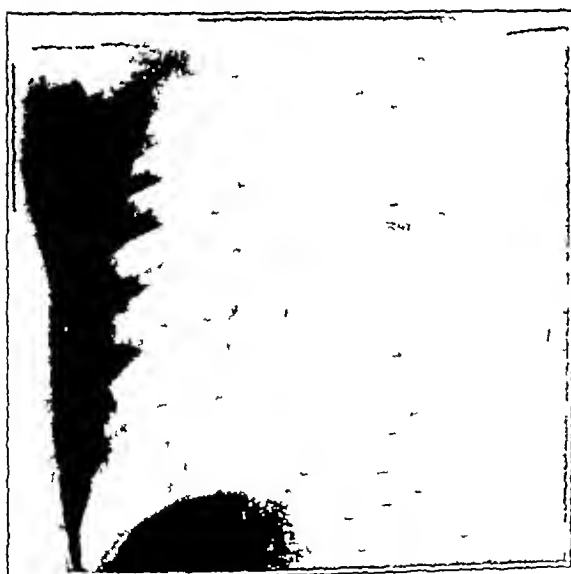


Figure 12

it is like an operation on a very ripe boil, the pus gushes out in a mass, and the situation is relieved. The patient recovered.

I had another case in which abscess of the lung developed following tonsillectomy. The patient was relieved after one evacuation of the abscess cavity. I should have been proud to have relieved him, but he did it himself. After a roentgenogram had been taken at the hospital, the patient went home to consider having bronchoscopy performed, but during an attack of coughing he coughed up the abscess



Fig 7—Effect of too much iodized oil. This illustrates the same case as does figure 6.

When he came back in two weeks, there was no trace of the abscess in the lung. Sometimes patients can be relieved by one evacuation.

The next case was one that occurred in a patient at the other end of the scale of age. A child, aged 2 years, had had a tonsillectomy performed twenty-one days before the roentgenogram shown in figure 1 was taken. A large abscess was found in the lower lobe of the right lung, without contents. Bronchoscopy was performed at once. A week after the roentgenogram was taken, rapid resolution occurred.



Fig 14 (case 52, table 3)—Unresolved pneumonia six weeks after onset  
Early peribronchial signs are seen in the lower lobe of the right lung



Fig 15—Later peribronchial signs three years and five months after onset  
the same patient as in figure 14



The temperature curve is shown in figure 2 After bronchoscopy was performed there was some disturbance in the temperature, but then it went down to normal and the child made an uninterrupted recovery

The essential point is to treat the patients early, while there is still elasticity in the wall of the abscess cavity and chance for it to contract

The next case was that of a child, aged 9 A tonsillectomy had been performed thirty-three days before admission to the hospital, when she was admitted she had an abscess and the type of temperature shown



Fig 10—Abscess of the lower lobe of the right lung following gassing during the war

in figure 3 Bronchoscopy was performed The temperature promptly subsided to normal, and the patient promptly recovered

The probability is that these are cases for aspiration, and that the focus lies near the hilum where it can be reached with the bronchoscopic tube

The next case was that of a boy who had had a tonsillectomy performed forty-two days before admission to the hospital He was in a miserable condition, the lesion was in the upper lobe of the right lung, that is, not so near the hilum, and rather close to the periphery The

TABLE 3—Detailed Analysis of Cases of Apparently Unresolved Pneumonia

[illegible]

In figure 6 the upper lobe of the right lung is shown, and the indication is that the bronchus of the upper lobe, where it entered the old abscess cavity, has been shut off by the scar tissue and the air, if it finds its way to that location, it is doing so through small collateral bronchi. In figure 7 a little more iodized oil was administered in order to fill out the cavity, and the whole picture was spoiled



Fig 12—Small postpneumonic abscess in lower lobe of the left lung

The next case was one that I consider proves the point that bronchoscopy should be performed in every case of abscess of the lung, for here seemingly was a lesion which was hopeless from the point of view of any but surgical treatment. There was interlobar empyema and abscess cavity of the lung. In spite of the gloomy outlook, the patient improved under medical treatment until the infiltration in the lung began to reappear, then bronchoscopy was performed, following bronchoscopy, the lesion diminished again, and the patient continued to improve. In March, 1926, she was clinically well. However gloomy

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think that it was possible to cure the patient because a spiral tube could be put right into the abscess cavity. The treatment consisted of injections of a silver preparation once a week, which seemed to have a disinfecting effect and made it possible to aspirate the abscess and keep it clean. I do not believe that the patient will be altogether safe from a recurrence. I do not see how a patient could ever be completely cured when the lung was the site of suppuration for such a long time.

FRANKLIN HOSPITAL FRANKLIN N. J.  
(SURGICAL CHART)

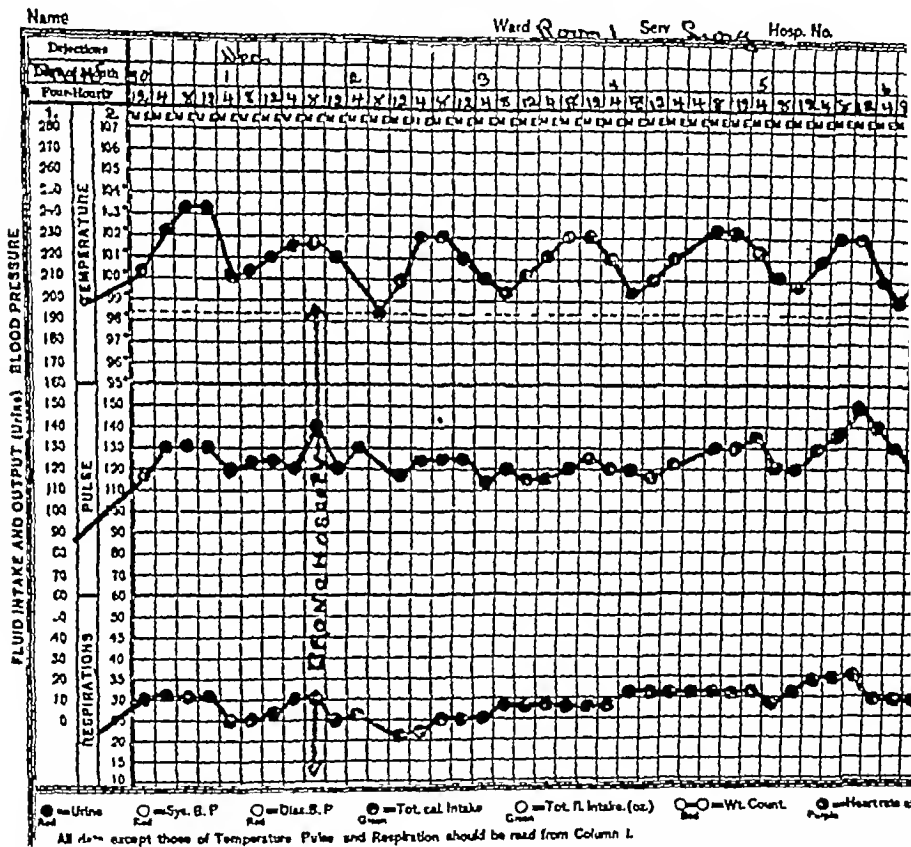


Fig. 14—Temperature chart of a very sick patient showing shock before bronchoscopy.

The next case is of a different type (fig. 10). The patient was gassed in the war and never completely recovered his health. Before coming to the hospital, he became conscious of a dry sensation in his throat and began to cough and sweat at night. He changed his work several times, and finally went to a hospital. He was admitted in July, 1925, and a short time afterward, bronchoscopic treatment was instituted. The temperature curve and the sputum curve are shown in figure 11. A large quantity of sputum was raised, up to 1,400 cc a day. On the day bronchoscopy was performed, only 800 cc was raised, but the day following it increased to 1,700 cc, because the al-

## TERMINOLOGY

It is not necessary to define pathologic conditions but I shall give brief explanations of what is meant by the terminology in certain procedures

**Drainage** The emptying of the products of infection directly through the wall of the chest

**Pneumonotomy** An incision or other opening made into infected tissue of the lung in which there is no gross collection of pus

**Bronchostomy** The deliberate opening of the bronchus whether directly or through an abscess cavity, together with the attempted maintenance of a passage from the bronchus through the wall of the chest

**Pneumonolysis** A procedure by which a lung, in part or in whole is directly mobilized or compressed or both whether from without or within the pleural sac, by operation This method is usually applied in upper lobe disease (apicolysis)

**Thoracoplasty** An operation on the thoracic cage intended to reduce the size of the hemithorax and to produce other mechanical changes within the chest

Any other procedures which may be mentioned are made clear by their titles

## CAUSES OF DEATH

In assigning the cause of death, the final operation usually but not invariably, appeared to have had most to do with the fatal termination except in rare instances, death will be ascribed to this operation Thus in the case of a patient who has had several previous operations these are not necessarily referred to but the procedure which seems to have had the determining influence will be mentioned As an example a patient with bronchiectatic and other suppurations of a lower lobe who has been subjected to avulsion of the phrenic nerve and graded thoracoplasty without improvement, dies of recurrent hemorrhages following pneumonotomy with the establishment of a bronchial fistula The cause of death is listed under bronchostomy this being the final operation and the probable cause of the fatal hemorrhages

Before operation every patient was suffering from a suppurative condition of the lung which presented phenomenon of systemic toxemia

Of the 105 cases 46 were acute and 59 chronic The designation of chronicity is not an arbitrary one reckoned by weeks or months but the history of each case was examined and the designation applied according to the impression made Twenty-five of the forty-six acute cases were fatal and twenty-two of the fifty-nine chronic cases

A number of patients were referred to me for surgical treatment but operation was not performed Several of the operations were under postural and other treatment and a number died of complications of hemoptysis I shall refer to only operative cases

# NONTUBERCULOUS BRONCHOPULMONARY SUPPURATIVE LESIONS

RESULTS OF TREATMENT BY ARTIFICIAL PNEUMOTHORAX \*

WYMAN WHITTEMORE, M D

AND

GERARDO M BALBONI, M D

BOSTON

Because of the great divergence of opinion in regard to the value of artificial pneumothorax in the treatment of patients with nontuberculous bronchopulmonary infections, and because of the lack of agreement as to how long the treatment should be kept up in order to produce satisfactory results, a discussion of the subject might not be unwelcome at this time

In an endeavor to arrive at some definite idea as to the actual value of this method of treatment in cases of suppurative infections of the lung, one of us (Balboni) has made an intensive search of the world's literature on this subject covering the last twenty-four years. All the references and abstracts of each report are published with this paper.

It has been a difficult matter to determine just what definite results many authors have obtained, and difficult or impossible to tell in what classification certain of their cases belong.

We have added twenty-three of our own cases taken from the Massachusetts General Hospital and the Peter Bent Brigham Hospital, Boston.

In our own series, which cover approximately seven years, there were eighteen cases of abscess of the lung, and five of bronchiectasis. The results were briefly as follows:

Artificial pneumothorax was attempted in eighteen cases of abscess of the lung. Two patients were completely cured and remained so, the treatment being kept up twenty-four and fifteen weeks, respectively. In two cases, there was temporary improvement (one patient died a year later of bronchopneumonia). Partial pneumothorax brought about improvement in all the symptoms in one patient, fifteen months after the suspension of the pneumothorax, the patient died of an embolus. There have been three deaths due to hemorrhage from the lung during treatment. In these three cases, a partial pneumothorax was created, but the lobe from which the bleeding came was adherent either to the wall of the chest or to the diaphragm, and pneumothorax was ineffective.

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\* From the Medical and Surgical Service of the Massachusetts General Hospital

(b) *Bacterial Embolism*—It is more difficult to avoid than air embolism, but an operation in which the pulmonary venous trunks are closed by ligature before the indurated tissue is wounded is not apt to be followed by septic embolism. This method is rarely if ever followed except in lobectomy, which will not be considered here.

It is easily conceivable that cerebral infection is liable to follow cauterization of the lung at the time when the sloughs are cast off. It must not be overlooked, however, that suppurative metastases to the brain may occur even without operation.

*Hemorrhage*—Fatal bleeding is fortunately not often encountered during an operation. It is, however, common during the postoperative period, and may occur months or even years afterward. It is a particularly dangerous accident, because in spite of packing massive hemoptysis is apt to drown the patient.

Although Dr. Graham, in his interesting work on the destruction of pulmonary tissue by actual cautery, depends on the low pressure in the lesser circulation to aid in hemostasis, the danger of hemoptysis has been very real in my own experience.

*Mediastinitis*—Only one of my patients succumbed to this complication. It followed an attempt to ligate a large branch of the pulmonary artery near the hilum through indurated tissue of the lung.

*Diagnostic Puncture*—There were two cases in which death followed diagnostic puncture of an abscess of the lung. Puncture in each instance was made before the patient entered the surgical service, and by the time he was seen by me there was extensive putrid phlegmon throughout the muscle planes of the back. Diagnostic puncture of the lung, except as a preliminary to immediate operation, should never be performed.

*Contralateral Conditions of the Lung*—There were seven cases in which death followed contralateral conditions of the lungs, including pneumonia, edema and abscess. While it is difficult to be certain that abscess was not present in the opposite lung before operation, edema and pneumonia as postoperative complications are well known and not always explainable. Massive collapse has also been reported.

*Postoperative Sepsis*—In sixteen cases death occurred from postoperative sepsis.

*Shock*—In two cases cardiac collapse and death occurred shortly after the operation.

*Acute Nephritis*—Death occurred in one case in which nephritis had not been known to be affected before the operation. At the time the thorax was progressing normally. Whether this was a separate disease or had something to do with the operation is impossible to state, since examination was not made.



TABLE 1—*Authors' Series of Cases of Abscess of the Lung*

Case	Duration of Disease	Pneumothorax	Complications	Operation	Result
1	6 months	Partial 10 months	Adhesions	0	Improved at first, died 15 months later of embolus
2	4 months	Partial, 3 months	Sterile fluid, adhesions	Aspiration of fluid	Slight improvement, died a year later from bronchopneumonia
3	2 weeks	Partial 2 weeks	0	0	Reported well one year later
4	2 years	Partial 3 months	Sterile fluid, adhesions	Thoracotomy	Sepsis, died
5	14 months	Partial 4 months	Sterile fluid, adhesions	Phrenic neurectomy	Cured
6	2 months	Failed, none	Abscess of the brain	None	Died
7	5 months	Partial 2 weeks	Adhesions, rupture, empyema	Rib resection drainage	Cured by operation
8	16 months	Failed, none	0	0	No change
9	5 months	Partial, 2 weeks	Adhesions	0	No change
10	2 weeks	Failed, none	0	Resection of rib and drainage	Marked improvement, later reported well
11	1 week	Partial, 2 weeks	Adhesions	Drainage of abscess	Improved by operation
12	3 months	Partial, 1 week	Adhesions, rupture, empyema	Rib resection, drainage	Cured by operation
13	3 months	Partial, 5 days	Adhesions, rupture, empyema	Rib resection, drainage	Cured by operation
14	1 year	Partial, 6 days	Adhesions, rupture, empyema	Rib resection, drainage of pleura and abscess	Improved by operation, still under treatment
15	8 months	Partial 3 months	Adhesions	None	Sudden fatal hemorrhage
16	1 year	Partial 4 hours	Adhesions	Operation and drainage of abscess	Sudden fatal hemorrhage
17	5 weeks	Partial, 2 weeks	Adhesions	None	Sudden fatal hemorrhage
18	4 weeks	Complete, 15 weeks	0	0	Cured

TABLE 2—*Authors' Series of Cases of Bronchiectasis*

Case	Cured	Weeks of Treatment	Improved	No Improvement	Failure to Produce Pneumothorax	Complications		Died
						Sterile Pleural Effusions	Empyema	
1	1	90				1		
2					1			
3					1			
4		52		1			1	1 (Following operation)
5		28	1	Still under treatment		1		
	1		1	1	2	2	1	1

## CHOICE OF PROCEDURE

*Artificial Pneumothorax*—This method finds its principal application in cases of abscess discharging by bronchus and in the earlier stages before the formation of a too rigid wall. I say this in spite of the fact that a few cases have been reported in which the disease had lasted a long time. In one reported by Forlanini, the final cure of a chronic putrid abscess took place after two years of treatment.<sup>1</sup> This isolated case should not, however, be held as an example especially in view of the dangers always present in this form of therapy. Patients with abscess of the lung not accompanied by too great bronchial dilatation may recover without treatment of any kind, this should always be borne in mind, especially when the physician is dealing with patients afflicted with some other serious illness.

*Thoracoplasty*—When thoracoplasty is performed there is a good chance for relief or clinical cure when the disease is of long duration and when fibrocavernous and bronchiectatic changes have occurred in an entire lung, and the opposite lung is healthy. There are two principal causes for the failure of this method (1) interference with the drainage of a cavity by the collapse itself and (2) the failure of the wall of the chest to obliterate the abscess cavities on account of the rigidity of their walls. Cough and expectoration continue or may become aggravated, or the condition may become acute, so that further operative procedures such as drainage will be required.

*Extrapleural Pneumonolysis*—This is a valuable procedure in certain cases of apical disease in which there are few or no pathologic changes in the remainder of the lung. By direct pressure, even the rigid walls of the abscess may sometimes be collapsed.

*Intrapleural Pneumonolysis*—Intrapleural pneumonolysis has seldom been performed deliberately. It has been successful in two of my cases in which it was done only because the employment of any other procedure did not seem possible after the chest had been opened.

*Drainage*—Drainage as an operation of choice in chronic cavitary abscess has proved its efficacy in many instances. It is more likely to succeed when a connection with the bronchial tree is either direct or small, because then expiratory effort tends to approximate the wall of the abscess. It is merely the modification of the usual surgical procedure for evacuating pus from a suppurating area.

*Pneumonotomy*—I have found pneumonotomy of value only in cases of indurated lung usually when there are numerous small abscesses resembling the structure of carbuncle. As the disease

<sup>1</sup> Garre and Quincke, *Munch. med. Wochenschr.*, 1890, 17, 1017.  
Surgery of the Lung, ed. 2, tr. n. New York, N. Y., 1900, p. 101.

TABLE 3—Cases of Abscess of the Lung Taken from the Literature

Author	Case	Duration of Disease	Pneumothorax	Complications	Other Treatment	Operation	Result	Comment
Riva Roel, 1903	1	3 months	Partial	0	0	0	Cured	
Forlanini, 1910	1	6 years	Almost complete, 1½ years	0	0	0	Cured	Well 4 years later
A Schmidt, 1910	3	?	1 partial	0	0	0	Cured	
			1 partial	0	0	0	?	
Wellman, 1910	2	?	1 partial	0	0	0		
			1 more extensive	0	0	0	Not improved	Pneumothorax abandoned After a fit of coughing, expelled 1,200 cc foul sputum, recovery
Volhard, 1912	1	?	Partial				Died	
Lowenhjelm, 1912	1	Months	Partial	Infection of other lung, 0	0	Withdrawal of air 0	Died	
Izar, 1913	2	?	Partial	0	0	0	Not improved	
			Complete	0	0	0	1 cured	
Kling and Mills, 1913	1	Months	Partial	0	0	0	Died	
Fornaen, 1913	1	1 year	Cough, 9 months	0	0	0	Cured	
Balboni, 1914	2	6 months	Almost complete, 6 months	0	0	0	Cured	
R C Matson	1	1 year	Partial	Cough worse	0	0	Not improved	Six months later, died
	2	1 week	Complete, 8 months	0	0	0	1 no benefit	
			Partial	0	0	0	Cured	
Webb and Gilbert, 1914	2	Short time	Complete	0	0	0	Improved	Abscess secondary to foreign body, expelled
			Complete	0	0	0	Cured	
Centani and Arena, 1914	1	3 months	Partial	Bad general condition	0	0	Died	
			Partial, 3 months	update		Aspiration of fluid 0	Cured	Six months after suspension of treatment, reported well
Reichman, 1915	1	2 months	Complete, 1 month	None	0	0	Cured	
Lauret and Hubert, 1914	3	8 months	Complete	0	0	0	3 cured	
Lindwall, 1915	1	1 year	Partial, 4 months	Syphilis	Mercury	0	Cured	
Epifano, 1916	1	4 months	Complete, 4 months	0	0	0	Cured	
Antonucci, 1916	1	3 months	Partial, 1 month	0	0	0	Cured	
Greer, 1916	1		Complete, 1 month	0	0	0	Worse	Well several months after complete reexpansion
Tewksbury	14	1 to few weeks	8 months, 2 partial	1 empyema, 1 labor	0	0	Cured	Interlobar empyema communicating with bronchus All these patients were treated early
			Complete	0	0	0	2 no improvement, 9 cured, 3 died	
Simon and Sweeney, 1918-1910	1	2 years	Complete	0	0	0	Cured	
De Verblion and Loiseau, 1918	1	3 weeks	Complete	0	0	0	Cured	
Well and Loiseau	2	?	Almost complete	0, 1 pericarditis	0	0	1 cured, 1 died	
Klinkert, 1918	1	6 months	Complete, 3 months	0	0	0	Cured	
Wessler, 1919	2	?	Partial	Extension of disease	0	0	Died	Four months after last injection, reported well
								In these two cases there was extension of the disease and patients died suddenly after last insufflation
Brundage, 1919	1	Weeks	Partial, 1 month	Empyema	0	0	Died	
Bergman, 1919	5	?	3 complete 2 none	0	0	0	3 cured 1 died 1 worse	

The following case shows the hazards always present in pulmonary suppurative lesions

Lina R., aged 21, had a putrid abscess following tonsillectomy. Drainage with permanent bronchial fistula was secured, and the patient was well satisfied with the result, refusing further operation to close the stoma. As a protection she wore a light piece of gauze pinned to her undergarment, except when she caught cold and a mucopurulent discharge appeared.

Four and a half years later, there was a hemorrhage from the stoma. It was checked by packing. During the first stage of an operation to prevent a recurrence of the bleeding, she died of cerebral air embolism.

Before deciding on a major surgical procedure all other methods reasonably promising relief should have been tried and examination by roentgen ray and bronchoscopy should have been made.

After most operations resulting in a chronic or permanent opening in the wall of the chest, a state of seminvalidism follows, even though the patient may be able to work. Accidents, such as a lighting up the disease with an extension of the gangrenous process and hemorrhage are apt to occur.

Much has been written on the question of the propriety of operating in chronic and in acute cases. Miller and Lambert, after an extensive experience, conclude that operation in cases of acute putrid abscess is unsafe, but that the drainage of chronic abscess is justified. No one can say, however, which acute abscess will become chronic, and progressive gangrenous suppuration cannot be permitted to go on without some incisive attempt to check it. Doubtless, operative statistics will suffer if operation is performed for acute abscesses, but if some patients are saved who might otherwise perish, operation is justified.

This discussion would be incomplete without a comparison with lobectomy. I feel that this operation has not had the attention which it deserves, and I am glad to note in the literature that there appears to be a movement in favor of the complete extirpation of a diseased suppurating lobe in suitable cases (Eloesser). The latest encouraging reference to lobectomy which has come to my notice is to be found in the Proceedings of the Staff Meeting of the Mayo Clinic for March 2, 1927 in which S. W. Harrington reports that Sauerbruch is performing the operation in stages. It is probably true that the technique of lobectomy as I have performed it in one or at the most two stages is the most improved. Certainly those of my patients who have had complete recoveries after lobectomy are more nearly normal both as to appearance and as to body symmetry than could be expected after any other procedure for similar pathologic conditions, and as I have stated in my paper<sup>2</sup> the vital capacity as shown by spirometer is not

<sup>2</sup> Lilienthal Howard: Vital Capacity and Body Symmetry after Lobectomy. *Ann. Surg.* 1926, 82: 286 (Jan) 1926.

TABLE 4—Cases of Bronchiectasis Taken from the Literature

Author	Cases	Duration of Disease	Pneumothorax	Complications	Other treatment	Operation	Result	Comment
Riva Rocci Brauer, 1896	2 4	4 years 3 years 10 years 22 years 6 years	Complete, 1 year Partial, 4 months Partial, 1 month Complete, 2½ months None	0 1 radiate 0 Pleural cavity obliterated	0 0 0 0	Rib resection 0 0 0	Cured Slight improvement Improvement Slight improvement None	No subsequent history, bilateral ease Improvement during treatment Treatment given up
A Schmidt, 1908	4	Several years	Partial, 3 months 1 none	0 Pleural cavity obliterated	0 0	0 0	None None	Three unilateral, results negative One bilateral
Oscar Frank v Jagle, 1910	1	Years	Partial, 1 month	0	0	0	Marked improvement	Still under treatment at time of publication
Wellman, 1910	1	Years	Almost complete	0	0	0	Marked improvement	Unilateral ease, year later about the same
Luxemborg, 1910	1	1 year	Almost complete, 2½ months	0	0	Plastic operation	Slight improvement	Unilateral ease, short duration treatment
Brauns, 1912	3	Years	Complete	0	0	0	2 cured 1 improved	Unilateral Bilateral, still under treatment at time of publication Unilateral
Volhard, 1912	1	Years	Partial	0	0	0	Marked improvement	
Kellar, 1912	4	13 years	One side, then the other	Adhesions	0	0	Died	
		4 years 1½ years 4 years	Complete, 1 month Complete, 1 month	0 0	0 0	0 0	No effect Improvement Marked improvement	Bilateral Bilateral, able to do full time work 2½ years later Bilateral
Koniger, 1912	2	Years	Partial	0	0	0	Improvement	Later results not known
Hochhaus, 1912	4	Years	1 partial 3 none	0 0	0 0	0 0	Improvement Improvement None	
Pekunovles, 1913	1	Years	Partial	0	0	0	Slight improvement	
Penzoldt, 1913	1	Years	Partial	Pleural infection	0	Thoracotomy	Cured	No later results reported
G Singer, 1913	3	Years	2 none, 1 partial, week	0	0	0	Improvement	
Zink, 1913	1	3 years	Partial, 10 months	0	0	0	Improvement	
Angelini, 1913	1	3½ years	Partial	Rupture of cavity	0	0	Died	
Riesdicker and Vogt, 1913	4	1 year 2 years 3 years 4 years 1 years	Partial None None 1 partial 1 year 1 complete	0 Adhesions 0	0 Adhesion	0 Rib resection draining cavity	3 slightly improved None 0 Improvement	Bilateral ease, slight improvement with pneumothorax, abscess cavity 1 year later One year after treatment died, pneumonia
R O Matson, 1914	2	Years	1 complete	0	0	0	Marked improvement	
Balboni, 1914	2							

# ABSCESS OF THE LUNG RELIEVED BY BRONCHOSCOPY

## REPORT OF CASES

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I have entitled my paper "Abscess of the Lung Relieved by Bronchoscopy" because I, like others, have been disappointed in the results of this treatment. Some patients whom I thought were cured were not. One patient who was cured of cough and who was free from symptoms later developed abscess of the brain and died. After a free interval of two years, another patient had a hemorrhage and an operation was necessary.

As to etiology, twenty of 103 cases that I have seen in the last two years and a half had no clear cause. It is sometimes difficult to find the cause; the patients say that they had had pneumonia or had been in poor health for a year or two and then began to cough up sputum. I have listed the causes in the table.

*Conditions Which Preceded Abscess of the Lung*

No conditions known	20
Pleurisy	6
Pneumonia	12
Tonsillectomy	27
Operation for appendicitis	2
Operation for hernia	2
Submersion	3
Operation for scirrhus	1
Exposure to gas during war	1
Colds, exposure and chill	3
Congestion of the lungs	1
Bronchitis	5
Influenza	1
Indefinite operations	5
Foreign bodies	9

In this table the incidence of abscess of the lung after tonsillectomy does not approach that reported by Dr. C. C. ...

As a rule cases in which foreign bodies were retained are considered cases of abscess of the lung for developmental purposes. The following cases were those in which the foreign body was retained for a long time: cases in which it was retained for four, seven, nine and twenty-three years. In one case wood was present for four years, in another case for seven years, in a case in which a piece of glass was

Fluid will develop at some time or other during treatment by pneumothorax whether the case is tuberculous or nontuberculous. There may be a small amount of fluid that can be perceived only by the fluoroscope.

#### SUMMARY

It seems fair to say that the patient with abscess who stands the best chance of being cured by artificial pneumothorax is the one in whom the following conditions are fulfilled, (1) the abscess is situated centrally, (2) it communicates with a bronchus, (3) the treatment is established within three or four months from the onset of the disease, (4) a complete or almost complete collapse can be obtained, (5) the treatment can be kept up between three and four months, and (6) artificial pneumothorax is not an indifferent procedure.

#### REPORT OF CASES

CASE 1—M. P., a fairly well developed Italian girl, aged 21, had had a cough of six months' duration which developed following a cold. She raised a large quantity of foul sputum in which there was blood at times, and she had had night sweats and chills and had felt weak.

The sputum was negative for tubercle bacilli. Roentgen-ray examination showed an area of dullness around the second and fourth ribs on the right side which extended across the chest from the roots of the lung to the axillary border. The dullness was of an even density except at the borders, where there was some mottling. The apices were clear.

The pathologic process at the base of the upper lobe of the right lung was diagnosed abscess of the lung.

Artificial pneumothorax was kept up for ten months, when it was abandoned, as the lung was only partially collapsed, the upper lobe being adherent. There was improvement at first, but the patient died fifteen months later from an embolus.

CASE 2—F. E. O., a white girl, American, aged 19, single, an employee in a shoe factory, was admitted to the hospital on March 16, 1920. Four months before admission a tonsillectomy had been performed. The patient felt sick and had fever and weakness afterward. About one month later, a cough developed with considerable foul sputum, occasionally blood-streaked. During the second month after the operation, the condition improved, then she had a chill and a constant increase of symptoms. Three cups of sputum were expectorated daily. During the cough, pain was felt on the right side.

Physical examination showed that a bronchiectatic condition was probably involving the right lung. Roentgen-ray examination was made on March 18. The appearance of an extensive pneumonic process in the lower part of the right side of the chest suggested evidence of bronchiectasis and retraction of the part of the lung involved. Definite evidence of a cavity was not seen. The heart was considerably displaced to the right.

Artificial pneumothorax was performed on April 15, 575 cc of air being injected into the right pleural cavity. Roentgen-ray examination on the same day showed that the pneumothorax lay low on the right side. A sharp outline of a shadow below resembled the liver, and above it resembled the diaphragm.





A roentgen-ray examination on January 15 showed the outer margin of the dull area at the base of the right lung much more sharply defined and the total area of dullness diminished.

On January 17, the lower lobe of the right lung was fairly well collapsed. The area of pneumothorax was in the costophrenic angle. The upper part of the lung was completely expanded.

On January 24, 650 cc of air was injected with the pressure at +5 at the end of the injection. The patient coughed and raised sputum three times during the injection. She continued to do well. A roentgen-ray examination on January 25 showed a partial collapse of the base of the lung.

The treatment was discontinued because of lack of cooperation by the patient. In April 1923, a report by letter stated that the patient was well and working.

CASE 4—C T C, a man, aged 33, had a tonsillectomy performed on Aug 28, 1921, ten days later, he began to cough and raise foul yellow sputum, about one cup a day. In September, 1922, he had his first hemoptysis. In March, 1923, he had several slight hemorrhages and he had a severe one on May 22, 1923. He was admitted to the hospital on May 22, 1923.

His family history and past history were not unusual.

Physical examination showed a well developed and well nourished man, who raised a great deal of blood-tinged, yellow sputum, not particularly foul. There was dullness over the left apex, and many moist rales were heard throughout the left lung. Tactile fremitus and spoken and whispered voice were increased over the left side of the chest.

The diagnosis was abscess of the upper lobe of the left lung.

On May 28, 1923, following a hemorrhage of 700 cc of blood, artificial pneumothorax was performed, and 900 cc of air was injected into the left side of the chest. On May 30, 250 cc of air was injected, on June 5, 400 cc, on June 14, 350 cc, on June 19, 400 cc and on June 22, 350 cc. The patient raised blood-streaked sputum at this time.

On June 26, 250 cc of air was injected into the left side of the chest. On June 19, a roentgen-ray report showed an increase in the size of the pneumothorax. There appeared to be a clearing at the apex of the left lung and a collection of fluid at the base, the apex was not collapsed, and was adherent both posteriorly and laterally.

On June 30, 375 cc of air was put into the left pleural cavity, on July 7, 250 cc, on July 12, 150 cc, on July 13, a roentgenogram showed the upper lobe still adherent, the lower lobe collapsed, and more fluid in the pleural cavity. On July 14, 200 cc of straw-colored fluid was removed. Bacteria or tubercles were not found. On July 29, 500 cc of air was injected.

On August 3, the patient was discharged with his general condition much improved. The cough and sputum were less, the sputum was not foul, and the tests for tubercle bacilli were negative.

On August 9, the patient reentered the hospital, and 400 cc of air was put into the left pleural cavity. On the same date a roentgen-ray examination showed some reexpansion of the lung with several fluid levels at the base. The patient was discharged. He reported at the outdoor department in October and showed some improvement. He was advised to have an operation with resection of the rib and collapse of the lung.

On Jan 18, 1924, he reentered the hospital with definite dullness and absence of breath sounds, tactile fremitus and vocal fremitus over the greater part of the whole left side of the chest. Dullness was most marked at the apex. The patient asked us to perform an operation.

bronchoscopy he sat up on the table, said how well he felt and then fell back in a convulsion. He died in twenty-four hours, so that bronchoscopy is not without danger. At autopsy an embolus was found in the brain. I suppose that this death following bronchoscopy was immediately due to it, but that is only one death in many hundreds of bronchoscopies.

I wish to illustrate two points: (1) that the cases particularly favorable for bronchoscopy are those following tonsillectomy, and (2) that



Fig. 6.—Injection of iodized oil (40 per cent solution) into an abscess of the lung.

the earlier the patients are treated the better. The following cases will demonstrate these points.

This first case was on eighteen days after a tonsillectomy the patient developed an abscess in the upper lobe of the right lung, which was formed eleven days later. This was the first case in which bronchoscopy was performed, the abscess cavity was reached, the necrotic tissue collapsed. I suppose that this was the first case

angle The lung was somewhat expanded since the last roentgenogram was taken There was probably air in the apex, in the costophrenic angle and in the narrow region along the axillary border

On July 15, 600 cc of air was easily injected, and the sputum was seen to be decreasing Roentgen-ray examination showed the area of the lung to be smaller than before, but not completely collapsed

On July 23, 200 cc of air was injected The needle became plugged On August 3, 750 cc of air was injected Roentgen-ray examination on August 4 showed that the pneumothorax extended from the apex of the right lung to the base along the axillary margin, it was about 1 inch wide (2.5 cm) in its narrowest portion The dulness in the costophrenic angle suggested a small amount of fluid

The patient was discharged to a convalescent home to build up her general health In December, 1926, a letter stated that she did not have a cough and did not raise sputum

CASE 6—F. E. C., a man, aged 66, entered the hospital on April 13, 1923, he had had symptoms of duodenal ulcer for three years On April 23, a gastro-jejunostomy was performed On May 9, roentgen-ray examination of the chest showed signs suggestive of pneumonia at the base of the right lung

On June 11, the patient had a foul breath, but the sputum was not particularly foul Many rales were heard throughout the back Artificial pneumothorax was performed 200 cc of air being injected On June 12, 200 cc of nitrogen was injected, on June 13, 350 cc, on June 15, 400 cc and on June 22, 400 cc On June 25, roentgen-ray examination failed to show any evidence of pneumothorax On August 1, the patient's condition was unaltered, the sputum was still foul On August 9, the pulmonary signs were clearing up somewhat, and the appetite was excellent The patient was sitting up in a chair The temperature rose to 102 F On August 10, he became unconscious and died

Autopsy showed abscess of the lung pleurisy on the right side, healed duodenal ulcer and a healed gastro-jejunostomy passage

At autopsy, the right lung weighed 680 Gm It was mottled, and the upper lobe showed depression On section, an abscess that measured 3 cm in diameter was seen below these depressions It contained pus which had a foul odor and was surrounded by a gray, necrotic zone The lung tissue peripheral to this zone was congested Two smaller abscesses were seen in the middle lobe They were less extensive, and the reaction about them was less marked than that in the upper lobe The left lung weighed 800 Gm and was normal The pleura was attached to the right lung

CASE 7—E. H., a woman, aged 18, white, Finnish, single, without an occupation, was admitted to the hospital on Feb 14, 1923 Five months before admission her adenoids and tonsils had been removed A few days later, she had a cough and pain in the right side of the chest At that time a roentgen-ray examination showed a dense area in the third to fourth interspace near the periphery on the right side A month later, the lung had a more normal appearance with cavitation in a dense area In another month, roentgen-ray examination showed almost complete disappearance of the condition The third month later (i. e., after operation), the patient began to cough again, and had fever and night sweats Four months later (in January), she had a hemorrhage and lost 1 pint of blood The cough and sputum increased and the sputum again contained blood and pus

The physical examination showed a pathologic process in the right side of the chest On February 19, 650 cc of air was injected into the right side Roentgen-



There was frequent hemoptysis. The sputum was mucopurulent and foul. He had lost 22 pounds (10 Kg) during the three months in bed. Later he was up and about, but did not work, and he regained his normal weight.

Examination of the chest showed a diffuse pathologic condition involving both the upper and the lower lobe of the right lung. A bronchiectatic or bronchopneumonic process shown in the right lung by the roentgen ray was perhaps of the nature of an acute abscess formation. A distinct cavity formation was not seen.

On July 11, 500 cc of air was injected into the right side. Roentgen-ray examination did not show any evidence of air in the pleural cavity. Air was seen in the subcutaneous tissues. Treatment by pneumothorax was abandoned, as there was not a free pleural cavity. Antisyphilitic treatment did not cause any change in the picture of the lung.

Operation and drainage were suggested.

CASE 9—E. H., a woman, aged 27, white, Swedish, married, a housewife, was admitted to the hospital on March 22, 1923. Nineteen weeks before admission tonsillectomy was performed under ether anesthesia. Two weeks later, pain developed in the right shoulder followed first by a dry cough, then by abundant foul, brownish sputum, some hemoptysis, night sweats and considerable loss of weight.

Examination of the chest showed that the expansion was diminished, tactile and vocal fremitus, dullness, bronchial breathing and rales were present over the right apex down to the spine of the scapula behind and to the fourth rib in the front. Roentgen-ray examination showed definite evidence of a pathologic process in the upper lobe of the right lung. In the absence of demonstration of a cavity, there was no positive evidence that it was an abscess.

Artificial pneumothorax was instituted on March 26, 500 cc of air being injected into the right side. Roentgen-ray examination on March 27 gave evidence of considerable gas in the pleural space, but apparently the gas had not separated the lung from the wall of the chest in the axillary margin.

On March 31, 500 cc of air was easily injected. Roentgen-ray examination on April 2 showed an increase of air in the chest, but the lung was not separated from the axillary margin. On April 3, 500 cc of air was injected. There was still considerable cough and sputum. On April 11, 700 cc of air was injected. The symptoms did not improve. Roentgen-ray examination on April 12 showed that the lung was about half the normal size, with dense narrow bands (adhesions) across from the axillary margin to the wall of the chest.

Artificial pneumothorax was ineffectual. The condition remained about the same. Operation was not indicated.

CASE 10—J. C., a white man, aged 21, a Russian, single, a junk dealer, was admitted to the hospital on Aug. 3, 1923. He had been in an automobile accident two weeks before admission. His nose had been broken and set under ether anesthesia three days later. About one week later, he suddenly began to cough and expectorate a dark, thick, foul sputum, which had persisted, about one glassful being raised every day. The cough was worse when he lay on either side. He had had pain over the lower left side of the chest for about one week. Fever and sweats developed.

Physical examination of the chest revealed an abscess of the lung, probably situated midway down the left axilla, more anteriorly than posteriorly, although it could not be definitely localized. The patient was ill. There were 27,000 white blood cells. A roentgenogram on August 4 revealed an area of diminished density, which was probably an abscess formation with a large cavity containing fluid.

patient was coughing up considerable pus, and on bronchoscopy the pus was traced to the upper lobe of the right lung, as indicated in figure 4. After bronchoscopy, the patient made an uninterrupted recovery. It is now over two years since bronchoscopy was performed. He was operated on for suppuration in the paranasal sinuses, and tonsillectomy had also been performed. It has been necessary to direct the treatment to the antrums to allow him to recover his health. The course of the temperature is shown in figure 5, he did not have much fever, 100 F being the highest point. Bronchoscopy was performed when the temperature reached that point. The sputum line was running from

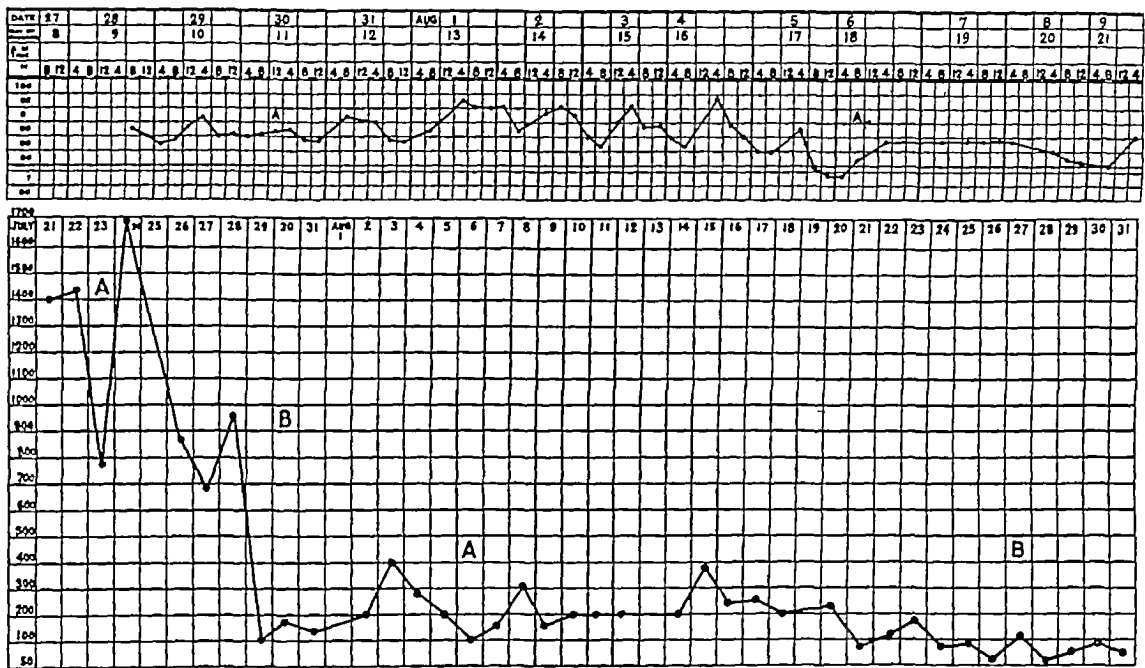


Fig 11—Sputum curve and temperature curve of patient shown in figure 10, A indicates performance of bronchoscopy, B, roentgen-ray examination

300 to 500 cc when the bronchoscopy was performed, the two bronchoscopies were all that was required to bring the sputum down to about 50, and he finally did not raise any sputum.

This abscess was of the same character as the other—a large single lobe abscess cavity located where it could be reached without much difficulty. Figure 6 shows the present situation in the boy's lung. This also illustrates the advantage of using iodized oil 40 per cent with fluoroscopy. It has always appeared reckless to me to pour into the lungs drugs of which one is not sure, moreover, too much of the iodized oil spoils the roentgenogram. The right amount can be exactly placed with the fluoroscope.

examination on April 4 showed practically the same picture as at the last observation, except that the density about the abscess cavity appeared slightly less. Pneumothorax seemed to have done little good. Roentgen-ray examination showed the possible danger of further performance of pneumothorax.

An exploratory thoracotomy was performed by Dr. Whittemore on April 9. A resection of the fourth and fifth ribs was made on the anterior axillary line. The lung was partially collapsed, but was held with a network of adhesions. Explorations showed an indurated area of the lung some distance posterior to the site of approach. The lower lobe was sutured in place in the wall of the chest, and a gauze wick was placed in the indurated area. On April 16, a resection of the seventh rib was performed at the posterior angle, the first stage wound was removed. A deep lying abscess of the lung, probably situated in the middle lobe near the hilum, was opened by finger dissection. A small amount of foul-smelling detritus was evacuated, and a rubber tube was inserted for drainage.

On May 4, distinct improvement was noted. The cough was less and the sputum was of a more glary and frothy character. Roentgen-ray examination on May 9 showed an area of dulness throughout the lower half of the right side of the chest, more dense at the base and along the axillary margin, where it obliterated the outline of the diaphragm and the shadow of the ribs. Its upper border corresponded with the lower border of the lung and fluid. The heart and left lung were normal.

On May 25, the patient was discharged to the outpatient department.

A second operation was performed in 1926. In March, 1927, he still coughed and raised purulent sputum and had a discharging sinus.

CASE 12—E. B. M., aged 29, entered the hospital on Feb. 25, 1924. Two months before, he had entered the hospital on account of pain and cough accompanied by the raising of a small amount of foul sputum each day. The cough was the result of tonsillectomy performed twelve days previous to entrance.

Examination showed rales in the second left interspace anteriorly. The temperature varied from 100 to 101 F. The foul sputum contained many cocci, but tubercle bacilli were not found.

Roentgen-ray examination showed a definite cavity with a fluid level at the second interspace. Artificial pneumothorax had been performed twenty-three and twenty-one days before admission. Roentgen-ray examination showed the lung almost completely collapsed after the second pneumothorax. Three days before entrance, 600 cc. of air was aspirated from the left pleural cavity. Two days before, pus was aspirated from the left pleural cavity. Drainage was performed and 1,200 cc. of pus was removed. The treatment then consisted of irrigation with a surgical solution of chlorinated soda. On March 16, the drainage tube was removed on account of pain. On March 21, resection of the rib was performed. On May 8, the drainage tubes were removed. On May 10, the patient was up in a wheel chair and walking about. On May 17, irrigation with a surgical solution of chlorinated soda was begun again and kept up until July 9, when the tubes were removed. The patient was discharged from the hospital on July 20.

On March 14, 1927, the patient's physician reported that she was completely well and did not have a cough or raise sputum.

CASE 13—A. P., an Italian girl, aged 17, was admitted to the hospital on March 29, 1924. Tonsillectomy had been performed under ether anesthesia sixteen days previously. Eleven days previously, she felt a pain in the chest. Six days later, fever and a slight cough developed accompanied by increased pain.

the outlook of the case may be from the point of roentgen-ray appearance, I think that bronchoscopy in every case should be performed in the hope that improvement may be effected

The next case was that of a man who had had an abscess for a year following a tonsillectomy. He had been in a hospital all that time. On examination, an abscess cavity was found close to the hilum, with dense fibrous tissue about it. This condition was different from that in the other cases which cleared up after one or two bronchoscopies had been performed. After the patient began to improve, bronchos-



Fig 13—Injection of iodized oil. This illustrates the same case as does figure 12

copies were performed during four months before he was finally in a condition to be discharged from the hospital. After the first bronchoscopy, the clinical improvement was remarkable. The temperature chart in figure 9 shows the temperature on admission and at the time when bronchoscopies were performed. Before the bronchoscopy there were 1,100 cc of sputum, and after two or three days the amount decreased and continued to be about 25 cc a day while the patient was in the hospital. That was three years ago, and now he is working on the traffic force and is apparently in the best of health. On account of the dense tissue, a long course of treatment was necessary. I



CASE 15—M L M, a man, aged 52, white, American, married, a milliner, was admitted to the hospital on June 2, 1923. Eight months before admission he began to have bronchitis with an unproductive cough. Three or four weeks later, he had high fever and expectorated a large amount of foul sputum, at times tinged with blood. Three months later, he went to Asheville, N. C., and four unsuccessful attempts were made by Dr. Ringer to produce artificial pneumothorax. He returned to Boston ten days before admission to the hospital.

Examination of the left side of the chest from the second to the fourth ribs showed an anterior area of bronchial breathing, with dullness and a few rales. There was little dullness over the corresponding posterior area. The rest of the lungs was normal. Roentgen-ray examination showed dullness of fairly even density on the left side from the apex to the angle of the scapula, with the exception of a bright spot in the first interspace with a suggestion of fluid level in it.

Artificial pneumothorax was performed. On May 19, 850 cc. of air was injected into the left axillary line near the fifth space. Roentgen-ray examination on May 21 showed partial collapse of the lower lobe and a considerable amount of air in the soft tissues of the wall of the chest. On May 22, 700 cc. of air was injected in the midaxillary line near the seventh space. The patient did not cough, and there was a slight sense of pressure. Roentgen-ray examination on May 24 showed marked increase in the area of the pneumothorax, which now occupied half of the lower part of the chest. The upper lobe of the left lung adhered broadly in the axilla. The pathologic area was about the same size.

Further compression with air seemed unwise. On May 27, exacerbation of temperature, cough and discomfort in the left side of the chest occurred. The patient was discharged on June 2, to be treated outside the hospital by Dr. Balboni. Pneumothorax was kept up for two months. The patient had a sudden fatal hemorrhage.

CASE 16—M B T, a white man, aged 27, was admitted to the hospital on Feb. 26, 1926.

In October, 1925, following bronchial pneumonia, a cough productive of foul expectoration developed. Occasionally, the patient raised a large amount of blood. Tubercle bacilli were not found in the sputum. Roentgen-ray examination showed a process suggestive of abscess at the root of the left lung.

On February, 1926, the patient's condition had not improved, but rather had lost ground, in that he was running a higher temperature at night and raising more sputum each day. Roentgen-ray examination at this time showed a definite abscess with a fluid level in the periphery of the right lung in the area between the third and fourth ribs in the axillary line. Examination of the sputum showed many streptococci, pneumococci, large and small bacilli and large spirochetes but no tubercle bacilli.

On March 1, resection of the third rib was performed under local anesthesia. The lung and pleura were adherent. The abscess was opened and drained. The patient made a fairly good convalescence following this operation, except that he continued to raise considerable amounts of sputum, drained large amounts from the abscess and had several small hemorrhages from the abscess, which were controlled with packing.

On October 6, the patient continued to raise some sputum, but had gained 10 or 15 pounds (4.4 or 6.8 Kg.) in weight and looked better than before the operation. Roentgen-ray examination showed a definite area in the region of the old abscess, but no fluid level. A month previous to this, the patient had been away and had allowed the drainage tube to come out, the sinus was completely healed.

cavity opened wide and the patient was able to empty it. In a few days, the amount of sputum fell to 100 cc. a day, there was a little recurrence and bronchoscopy was performed again, then the amount of sputum diminished and finally disappeared. The temperature curve was not as favorable as the sputum curve, it was discouraging. After the first bronchoscopy, the temperature was about 100 F. The patient was in poor condition when treatment was begun, and it required considerable courage to perform bronchoscopy again, but after the second time, he began to improve, and finally made a good recovery. There is still a good deal of scar tissue, but clinically, the patient is well and able to work and earn his living.

The next case was of a different type (fig. 12). The patient had had pneumonia three years previously, and after that was not well for two and a half years. Six months before admission to the hospital, he began to cough and perspire at night and felt miserable. The condition was discovered in the lower lobe of the left lung. The patient was a well nourished, obese man, with a good color and appeared to be in excellent health, yet he coughed all night and raised an ounce or so of sputum during the day. An attempt was made to bring out the lesion with iodized oil 40 per cent by injecting it through the trachea, but this resulted only in scattering it through the lung without any detail. The bronchoscope was passed under the fluoroscope, and by injection the character of the lesion could be demonstrated. I should say that the lesion appeared to be a sort of carbuncle of the lung—a mass of scar tissue with fistulous tracts. Bronchoscopy was performed for a year or so and finally a cure was effected.

It is sometimes asked whether it is not dangerous to perform bronchoscopy on sick persons who have been coughing, who are in poor condition, and who have a good deal of fever. The surgical chart of one of the patients who had an abscess following an appendectomy is shown in figure 14. Death resulted. The time of bronchoscopy is indicated on the chart. The next day, twenty-four hours later, there was a fall in the pulse rate, respiration and temperature. Shock did not result from the procedure, even though the patient was exceedingly sick at the time and could not lie down. So it can be said that shock does not follow bronchoscopy.

On February 16, he reentered the hospital, and on February 17, his appendix was removed under ether anesthesia. The pathologic report was fibrous appendix. The wound became infected and was irrigated with surgical solution of chlorinated soda. The patient had a slight septic temperature. Early in March, he began to cough and to raise sputum. Roentgen-ray examination showed a definite abscess of the lung with the fluid level in the left lobe.

On March 21, artificial pneumothorax was performed, and 700 cc of air was injected. On March 24, 400 cc was injected, on March 31, 400 cc and on April 4, 500 cc.

On March 17, he raised 150 cc of sputum, on March 19, 75 cc, on March 20, 50 cc, on March 21, 100 cc and on March 22, 20 cc. Tubercle bacilli were not found.

On April 3, roentgen-ray examination showed the lung well collapsed. The patient was discharged on April 19. Artificial pneumothorax was kept up for three months after the patient's discharge, and then the lung was allowed to expand. On March 15, 1927, the patient was well and free from cough or symptoms, the lung was fully expanded.

CASE 19—L. N., a school boy, aged 16, white, Jewish, was admitted to the hospital on Jan. 2, 1923.

Eight months before, his tonsils and adenoids were removed and also "bone from the left side of the nose." Since then he had had a dry cough for three months, then it increased, and he expectorated foul, green sputum. Lying on his back or on the left side aggravated the cough. He did not have fever, slept poorly, and had lost 5 pounds (2.3 Kg.) during the last four months.

Examination of the chest revealed that it was resonant throughout except for diminution in the apex and at the base of the left lung. Rales were not heard. Breath and voice sounds were transmitted normally. The fingers were slightly but definitely clubbed. The sputum did not show any tubercle bacilli.

On January 5, a roentgen-ray examination showed a rounded area of increased density with poorly defined borders and a bright spot in its center in the left side of the chest just above the shadow of the diaphragm and adjacent to the shadow of the heart. The area appeared larger with the patient's back to the screen. The left side of the diaphragm was seen faintly. Both apices were clear, and the right side of the diaphragm was regular. The diagnosis was bronchiectatic abscess.

Artificial pneumothorax was performed on January 9, and 800 cc of air was injected into the left side after three attempts. The patient's condition improved, the cough decreasing. Roentgen-ray examination on January 11 showed a small amount of gas in the lower part of the left side of the chest.

On January 12, 850 cc of air was injected, and on January 15 roentgen-ray examination showed that the lung was not completely collapsed.

On January 16, 900 cc of air was injected, and on January 17, roentgen-ray examination showed the entire left lung fairly well collapsed. The involved area at the base was distinctly smaller. On January 19, 900 cc of air was injected. The patient did not feel any discomfort, the sputum was less foul. Roentgen-ray examination on January 20 showed practically complete collapse of the lung. On January 25 and 27, air was injected. The patient's condition was much improved, and he was discharged to the outpatient department for further treatment.

Artificial pneumothorax was kept up until January, 1925. In March, 1925, the lung was fully expanded, the patient was well, and did not cough or raise sputum. On April 28, 1927, he was free from symptoms and was in good health.

Improvement did not occur in two cases, and in three, a satisfactory pneumothorax could not be produced. Empyema complicated the situation in five cases during the treatment. Operation was performed in all cases. Three patients were entirely cured by drainage, one is still under treatment, and one died. It seems questionable whether or not this is an ideal treatment in cases of abscess of the lung.

In the five cases of bronchiectasis, one patient was cured after eighty weeks and one is improved, but is still under treatment after twenty-eight weeks. In one case in which the condition was bilateral, pneumothorax was maintained on one side only. After fifty-two weeks, considerable improvement resulted, then an empyema developed, and death resulted several days after operation. In the other two cases, a satisfactory pneumothorax could not be produced.

In summarizing our own experience in cases of bronchiectasis, it seems fair to say that artificial pneumothorax offers only a small chance of cure, and in the successful cases it must be kept up for a long time. Nevertheless, it seems fair to attempt a pneumothorax in cases of bronchiectasis, as it will not contraindicate surgical intervention later if the pneumothorax should not be feasible or should not produce lasting benefit.

Cases from the literature will be reported in detailed tables. A short summary of the cases of abscess of the lung follows.

Of 129 cases collected, 68 patients (52 per cent) have been reported as cured, and 18 (14 per cent) have died. Empyema developed in 11 cases, and 6 of the patients were cured by operation. There was no improvement in 12 cases.

In the cases in which a cure was reported a complete or almost complete collapse was obtained, and in some of the failures the pleural cavity could not be entered or only a partial collapse was obtained. In the majority of these cases, the abscess was situated near the root of the lung and always communicated with a bronchus. In most of the cases, the disease had existed from one to four months when treatment was begun. The duration of treatment varied, ranging from a week in one case to one and a half years in another. It has been difficult to arrive at any definite conclusions as to how long artificial pneumothorax should be maintained. Many reporters fail to record the duration of the treatment, and those who do report it vary considerably in their accounts, one, three, four and five months were the most frequent periods, probably from three to four months is about the average.

This high percentage of reported cures is extraordinary to us in view of our own experience with this method of treatment. If we add our own 18 cases to the 127 in the literature, the percentage of cases in which cure was reported is slightly lower as out of 145 cases, cure was obtained in 68, or 48 per cent.

decreased. He would not consent to cutting the phrenic nerve. Treatment by pneumothorax was given up after four attempts. The pleural cavity was obliterated.

CASE 21—M. D. N. was admitted to the hospital on Aug. 23, 1923. In October, 1922, he had a severe cold in the chest accompanied by fever and cough. On December 19, the patient had another heavy cold in the chest which lasted up to the time of admission. He had considerable cough and raised sputum. There was a small amount of sputum at first, but this gradually increased until he raised a cupful a day. He had been unable to work since March. For two months, he had had a dull pain in the left side of the lower part of the abdomen.

Examination revealed that the heart was pulled to the right side. A few râles were heard in the upper part of the chest. Voice fremitus was increased slightly. On August 29, roentgen-ray examination showed a dull area of mottled character at the base of the right lung, it extended outward from the root of the lung and occupied the greater part of the right side of the lower part of the chest. Artificial pneumothorax was given. On September 20, roentgen-ray examination showed the right lung completely collapsed. On September 26, the patient was discharged from the hospital.

On Feb. 2, 1925, the patient reentered the hospital. Roentgen-ray examination showed an area of homogeneous dulness, entirely obscuring two thirds of the right lung, with a sharply defined upper border at the level of the third rib. The heart was displaced to the left. The appearance suggested hydropneumothorax of the right lung. Fluid was withdrawn again and replaced with air.

On February 5, roentgen-ray examination showed that the right side of the chest was filled with air. A small amount of fluid was seen at the base. On February 17, the patient was discharged.

On March 13, the patient had bronchiectasis. Pneumothorax was repeated, and the patient was discharged on March 16. On June 1, he reentered the hospital. Roentgen-ray examination showed a shadow corresponding to fluid in the right side of the chest and indicating hydropneumothorax. Fluid was withdrawn again and replaced with air. On June 3, 200 cc. of a greenish, cloudy fluid was aspirated, the vital capacity was 2,000 cc. On June 9, fluid was aspirated again, the vital capacity was 1,900 cc. The patient was feeling worse and coughed more. On June 13 and 21, the chest was aspirated. On July 1, the patient had a rise in temperature in the evening. On July 3, roentgen-ray examination showed complete collapse of the right lung. The chest was about one third full of fluid. The patient was discharged on July 15. Pneumothorax was continued for seventeen weeks.

On September 28, the patient reentered the hospital. Fluid was again demonstrated in the right side of the chest. Hydropneumothorax was performed. The patient was raising about 28 ounces (828 cc.) of foul greenish fluid during twenty-four hours. Three hundred cubic centimeters of thick, greenish fluid was aspirated from the chest. In October, 500 cc. was removed from the chest and on October 11, the patient was discharged. On November 10, he returned to the hospital. His condition was unimproved, and he was raising about six cupfuls of sputum each twenty-four hours. On November 19, he was discharged, but he returned to the hospital on November 27, and was discharged on December 9.

On Jan. 9, 1926, he returned to the hospital. He was still raising a large amount of sputum, and his condition was no better. On January 21, an operation was performed under local anesthesia for resection of the eighth rib. The

A brief summary of the cases of bronchiectasis follows

Ninety-three patients were treated by artificial pneumothorax, with fourteen (15 per cent) reported cured, forty-four were reported improved (varying from slight to really great improvement) Only seven patients were reported as having died, and of these, two died following thoracoplasty In twelve cases, pneumothorax could not be created There was a rupture into the pleural cavity in only three

In the patients who were cured the disease had existed for a length of time, varying from a few months to one year, with a few rare exceptions in which the disease was of two, three and four years' duration This bears out the point that every one recognizes, that if treatment is to produce satisfactory results, it should be established early

It seems extraordinary to us that of ninety-two patients, fifty-seven should be reported as improved by the treatment, and that it was impossible to enter the pleural cavity in only twelve

In the satisfactory cases in which a complete collapse could be brought about, the treatment was kept up for a period varying from five or six months to six years

A comparison of our own results with those taken from the literature is striking In cases of abscess of the lung we report only 2 patients of 18 (11 per cent) cured, whereas in 127 case reports collected from the literature, 66 (51 per cent) patients are reported cured In the cases of bronchiectasis, we report 1 cure out of 5, whereas of 92 cases taken from the literature, 14 (15 per cent) cures are reported In contrasting these figures, it should be borne in mind that it has been impossible for us to determine what the term "cured" meant to many of the reporters of cases Whether their patients have remained free from symptoms merely while under their observation or for a period of several years, we are unable to tell

If the statistics of cases of abscess of the lung which we have compiled from the literature are correct, and if we may expect a cure in 51 per cent or even in from 30 to 40 per cent of the cases in which this treatment is established early (at most three or four months from the beginning of the disease), it seems to us that this form of treatment should be used more frequently, in spite of our own experience of cure in only 11 per cent

We do not feel any great amount of confidence in the use of artificial pneumothorax in cases of bronchiectasis, although the literature reports a cure in 15 per cent of the cases, but we are willing to believe that in a rare case which is taken early and in which there are no adhesions, the patient may be cured We believe also that occasionally a patient may be kept almost free from symptoms for as long a time as a complete collapse of the lung can be maintained

patient was dismissed one month later as no improvement was noted. Examination two months later showed the patient to be in a fair condition. The amount of foul sputum had decreased. Pneumothorax was not demonstrable by the roentgen ray.

**Summary** This was an advanced case in which both lungs were affected and there were marked adhesions on the side on which operation had been performed, consequently there was only partial pneumothorax which resulted in a definite decrease of sputum. The improvement was slight. A subsequent history was not given.

The second case was that of a boy, aged 12, who had been ill many years and who had a long continued high fever. The process was on one side. The fingers were moderately clubbed. Ten insufflations were performed in four months. As a result, there was extensive pneumothorax without exudate, but there were two long, thin adhesions. The general condition was fairly good. Dyspnea was not present. Over the healthy lung in the lower part of the back were scattered moist râles. At the time this case was published, treatment was being continued.

**Summary** This was an old, one-sided case with moderate physical signs. Marked improvement occurred during a moderately long continued treatment by pneumothorax. Subsequent results were not known.

The third case was that of a woman, aged 38. One side of the lung had been affected for many years. Four insufflations were performed in nine weeks. As a result, the lung lay crumpled at the hilum. There was no exudate and little sputum.

**Summary** In this case of long standing one lung was affected, there were slight clinical and physical symptoms and little sputum was raised. Treatment by artificial pneumothorax brought about a good collapse of the lung and the expectoration of a slight amount of sputum. The subsequent history is unknown. The treatment was discontinued on account of diffuse pleural adhesions.

A pneumothorax could not be performed in the fourth case.

In 1910, Schmidt,<sup>3</sup> after an experience of five years, reported the treatment of eight patients with bronchiectasis and three with abscesses of the lung. He had treated some patients with infusions of oil and some with artificial pneumothorax.

In one of three cases of abscess of the lung, good results were obtained with artificial pneumothorax. There were four cases of bronchiectasis, three unilateral and one bilateral.

<sup>3</sup> Schmidt, A. Brauer's Beitr 9, no 3, 1908, Erfahrungen mit dem therapeutischen Pneumo- und Hydrothorax bei einseitiger Lungentuberkulose Bronchiectasien und Aspirations-Erkrankungen, Beitr z klin d Tuberk 9 261, 1908-1910.

Martin and Caldwell &  
Gilbert, 1920

Bluntresen Munte 1920

Annand, 1920

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White, 1921

Johnson, 1921

March, 1922

Plerry and Barber 1922  
Rich, 1922

Murrell 1929

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Trolser and Guyot 1923  
Pelle 1923  
Perkins

Perkins and Burrell, 1923

Heller, 1933

Hullbom and Church

Southey H. L. 1925,  
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Donnell and Churchill 1921  
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In 1910, Wellman<sup>6</sup> reported the treatment of two patients with abscess of the lung. Although one patient recovered following the attempted pneumothorax, the recovery cannot be ascribed to this method of treatment, as the lung was never compressed, even though the last manipulation ended in the discharge by mouth of 1,200 cc of purulent sputum. In the other case, the pneumothorax had to be discontinued, and the patient was discharged convalescent.

A case of bronchiectasis was reported in a girl, aged 19. The process was one-sided. She had been ill for years following pneumonia. Fifteen insufflations were performed in slightly less than one year. There was diffuse pneumothorax. The lung lay at the hilum, there were several stringy adhesions to the diaphragm. Râles were not present fifteen months after beginning the treatment, and the gas had entirely disappeared. There were still numerous râles over the lower lobe of the left lung. One year after the collapse therapy was employed, the patient was still able to do her work.

**Summary** In a case of chronic pneumonia of long duration with slight bronchiectasis and no debilitation, marked collapse of the lung was obtained, and as a result the sputum disappeared. After pneumothorax had existed one year, it suddenly "went back" and could not again be produced. There was marked improvement. A similar condition existed one year later.

In 1912, Volhard<sup>7</sup> obtained good results in a case of bronchiectasis. A patient with abscess of the lung improved after pneumothorax, but later the abscess infected the pleura, and fatal empyema resulted. According to Volhard, one cannot reckon on the pleural cavity remaining sterile in cases of abscesses of the lung, for this reason, such cases are not adapted to treatment by the method of pneumothorax.

In 1910, Luxemborg<sup>8</sup> reported a case of a patient, aged 28, who had an infection on one side of the lung of one year's duration. Five insufflations were given in two and three-fourths months. There was partial pneumothorax. At times the sputum decreased, but it never disappeared entirely. Therefore, plastic operation of the thorax was performed, with good results.

**Summary** The partial pneumothorax of short duration was only slightly successful in this probably advanced case with cavities, at least outside the hilum.

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6 Wellman. Klinische Erfahrungen in der Behandlung mittels kunstlichen Pneumothorax, Beitr. z. Klin. d. Tuberk. **17** 81, 1910.

7 Volhard. Ueber den kunstlichen Pneumothorax bei Lungentuberkulose und Bronchiectasien, Munchen med. Wchnschr., Aug. 6, 1912, no. 32, p. 1746.

8 Luxemborg, H. Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1910, vol. 21.

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Five hundred cubic centimeters of nitrogen was withdrawn from the pleural cavity. Bronchopneumonia developed at the base of the lung, and the patient died. Autopsy showed that the upper and lower lobes of the right lung were collapsed. The middle lobe was converted into a mass of connective tissue about the abscess cavity. There was an area of bronchopneumonia at the base of both lungs. In 1912, Kellar<sup>11</sup> reported two unilateral and two bilateral cases of bronchiectasis with improvement in two of the cases as a result of artificial pneumothorax.

The first case was that of a man, aged 30, who had had a cough since his seventeenth year, when he had had pneumonia of long duration. He had dyspnea. Pneumothorax was applied to one side, which proved to be the one less involved. Shortly afterward, pneumothorax was applied on the right side. Several insufflations were given, but were not successful. The patient died soon afterward.

**Summary** The process occurred on both sides following pneumonia of long duration without marked clinical symptoms. A brief attempt to apply pneumothorax was not successful owing to pleural adhesions.

In the second case, a man, aged 31, had had a cough for three or four years. There had been considerable sputum in the last few months. On the left side there was a large pneumothorax. Six insufflations were given without any effect on the sputum. Then the patient gave up the treatment.

**Summary** A short compression of a rather lightly infected lung through a very large yet not complete pneumothorax did not have any effect on the symptoms of the double process.

In the third case, a girl, aged 18, had had a cough for one and one-fourth years. Blood was present in the sputum eight months before she consulted Dr. Keller. There was complete pneumothorax. The number of times artificial pneumothorax was performed was not given. At the time of the publication of the case, treatment was being continued. There was complete collapse. The cough and sputum ceased only when the patient was given new insufflations every four weeks.

**Summary** Total pneumothorax caused the disappearance of symptoms in this one-sided but severe process, and the patient was able to do full time work two and one-fourth years later. The results were good.

The fourth case was that of a man, aged 32, who had been coughing since he had had pneumonia of long duration four years previously. The amount of sputum and dyspnea increased. The number of insuf-

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<sup>11</sup> Kellar. Brauer's Beitr, 1912, vol 22, no 2, Erfahrungen uber den künstlichen Pneumothorax, Beitr z klin d Tuberk 22 165-242, 1912.

or possibly the lower margin of the consolidated lung. A dulness was found throughout the lower half of the right side of the chest, and the appearance of gas was between the diaphragm and the liver.

On April 20, 600 cc of air was injected. The temperature dropped, but there was still considerable cough and sputum. A roentgen-ray examination showed partial collapse.

On April 24, 500 cc of air was injected. The patient's condition improved, and the cough and sputum decreased.

On May 1, 450 cc. of air was injected. A roentgen-ray examination on May 6 showed that the lung was completely collapsed. There were two areas in which the lung appeared adherent to the wall of the chest. On May 14, roentgen-ray examination showed that the diaphragm was apparently held up to the base of the lung by adhesion. Evidence of some subcutaneous emphysema was seen on the right side of the wall of the chest.

The patient was to report in two weeks.

On June 3, roentgen-ray examination showed the outline of the partially collapsed lung and the fluid level in the lower part of the chest.

On June 11, the chest was tapped, and 8 cc of slightly cloudy, straw-colored fluid was withdrawn. Roentgen-ray examination showed a definite area of dulness on the right side of the chest, which extended horizontally across the chest in the fourth interspace in front. The costal margin of the diaphragm appeared fixed. On rotation, the area of dulness appeared to be nearer the back than the front.

The patient died on July 1, 1921, of bronchopneumonia.

CASE 3—A N, a Polish woman, married, a housewife, aged 42, entered the hospital on Jan 6, 1923. She had had a pain in the right side of the chest for nine weeks, vomiting for four weeks and a cough for nine weeks.

A week before admission, she had swallowed a veal bone. The local physician recovered a small piece. Coughing and vomiting persisted so that the patient could not eat or sleep. The pain on the right side prevented her from lying on that side, the pain was worse on coughing. She expectorated foul, puslike sputum continuously and lost 35 pounds (15.9 Kg). The esophagus was not obstructed, and evidence of a foreign body was not found.

Physical examination showed that the expansion of the chest was equal. The upper sternum was prominent, the right axilla was slightly dull. There were a few fine râles low in the left axilla. Breath sounds and voice sounds were satisfactory.

On January 10, a roentgen-ray examination revealed dulness at the base of the right lung of mottled character with an indefinite outline which somewhat obscured the outline of the diaphragm. There were limited respiratory movements on this side. Root shadows on the right side were increased in size and in density. Markings running to the lower lobe also were prominent. The remainder of the fields of the lung were clear. The diaphragm on the left side was sharply defined, and the respiratory excursion was normal. There was no evidence of a cavity formation. The appearance suggested a rather extensive process of a pneumonic character involving the lower part of the lower lobe of the right lung.

On January 13, 500 cc of air was injected into the right midaxillary line, the needle was reinserted, and 100 cc more was given. A reaction did not occur. During the next three or four days there was much improvement and less coughing.

foul sputum. A complete collapse of the affected lung was induced, and the sputum was reduced to about 1 ounce daily. The patient had been under treatment for three months when examined. Three months later, he was in excellent condition, having only a slight cough and raising a small amount of sputum.

Izar also reported unsuccessful results in a young man, aged 19, with an abscess of the inferior lobe of the right lung. A partial pneumothorax was obtained, with the reduction of the sputum to one half. Attempts to collapse the lung where it was adherent posteriorly caused so much discomfort that the treatment had to be abandoned, leaving the patient in the same condition in which he entered the hospital.

In 1913, Singer<sup>17</sup> reported three cases in which artificial pneumothorax was attempted. He was unable to induce a pneumothorax in two cases on account of extensive adhesions.

In the third case, there was an extensive bilateral bronchiectasis with multiple loci. Marked improvement did not follow two injections of 1,000 cc of nitrogen into the left pleural cavity. Later injections were given on the right side, but no noteworthy change was noted.

In 1913, Angelini<sup>18</sup> reported unsuccessful results of pneumothorax therapy in a case of bronchiectasis of three and one-half years' duration. It was impossible to cause collapse of the lung even with high pressure on account of extensive adhesions. The patient became worse, and hemoptysis and pyothorax resulted from rupture of the cavity.

In 1913, Hochhaus<sup>19</sup> performed pneumothorax in four cases. In one there was marked improvement, in three, no improvement. Later results were not known.

In 1913, Pielsticker and Vogt<sup>20</sup> reported four cases of bronchiectasis in children aged 11, 6, 7 and 2, respectively. Treatments were unsuccessful in two of these cases because of adhesions, in one, the treatment was discontinued because of contralateral bronchitis and in the other because of the patient's refusal to continue treatment.

In 1914, Fornaca<sup>21</sup> reported the case of a woman, aged 40, with an abscess of one year's duration of the lower lobe of the left lung. The

17 Singer, G. Zur konservativen Behandlung der chronischen Lungenentzündungen, Verhandl d Kong f Inn Med 30 380, 1913, discussion by Bräuer, Penzoldt, Singer, p 395.

18 Angelini, A. I risultati immediati del pneumotorace artificiale alla Forlanini nei malati di tubercolosi polmonare nell'ospizio, Umberto I in Roma, Riv osp no 2 913, 1913.

19 Hochhaus. München med Wchnschr, 1913, p 385.

20 Pielsticker, F. H., and Vogt, H. Ueber künstlichen Pneumothorax bei Kindern. Kinderklinik Strassburg, Monatschr f Kinderh 11 143, 1913.

21 Fornaca, L. Ascesso polmonare per ingestione e permanenza d'un corpo estraneo trattato e guarito col pneumotorace artificiale, Pensiero med, 1913 p 143.

On January 19, a resection of the second and third ribs was performed.

On January 25, roentgen-ray examination showed a diffuse clouding about the upper half of the lung without definite evidence of a cavity.

On January 30, a resection of the second, third, fourth, fifth and six ribs was performed. On February 3, the wound became infected with streptococci and was opened and drained. The patient died on February 9.

Autopsy showed abscesses of the lung, atelectasis, bronchitis, chronic adhesive pleurisy and fibrosis of the lung.

CASE 5—V G W, a woman, aged 31, white, married, American, without an occupation, was admitted to the hospital on April 28, 1923. Following an operation fourteen months before for suspension of the uterus, removal of an abscessed ovary and appendix, a dry cough developed. Later thick, foul, greenish sputum was observed. The patient was in the Rutland Sanitarium five months before for prevention of tuberculosis. The sputum gradually increased. Roentgen-ray examination on May 1 showed a definite area of mottled density obliterating the angle between the diaphragm and the right side of the heart. A margin of the dull area was indistinct, and a definite cavity was not seen. Both apexes and the left lung were clear. A rather extensive pathologic process was seen near the right descending bronchus and confined to the lower lobe of the right lung, it was probably an abscess.

Examination of the chest showed fluid at the base of the right lung in the back, extending from just below the angle of the scapula downward. Tactile and voice fremitus and breath sounds were diminished over this area. The rest of the lungs were clear.

On May 10, 900 cc of air was injected into the fifth space in the midaxillary line on the right side. On May 12, a roentgenogram did not show any evidence of pneumothorax. On May 18, an unsuccessful attempt was made to inject air. On May 21, an exploratory thoracotomy was performed by Dr. Whittemore, who also resected the ninth rib. When the pleural cavity was opened the lung collapsed and there were no adhesions. The wound was closed without drainage, leaving the lung collapsed.

On May 23, 450 cc of air was injected, and on the same date a roentgenogram showed the lung partially collapsed. On May 25, 600 cc of air was injected. The patient coughed less, and improvement followed. On May 28, 550 cc of air was injected. The foot of the bed was elevated, and the patient lay on his left side to help drainage. A roentgen-ray examination on this date showed the upper and middle lobe completely collapsed. The lower lobe appeared to be adherent along the diaphragm or in the axillary line close to the diaphragm.

On June 1, 600 cc of air was injected. There was considerable coughing at the end of the injection and the sputum was becoming thinner.

On June 5, 250 cc of air was injected. The treatment was stopped because the patient coughed considerably while it was being given. There was a great deal of air in the tissues. A roentgen-ray examination showed practically the same condition as before without evidence of fluid in the tissue.

On June 13, 650 cc of air was easily injected. On June 22 575 cc was injected, during the injection, there was an annoying cough. On July 9, phrenic neurotomy was performed by Dr. Porter to paralyze the right side of the diaphragm and to help to collapse the right side of the chest. Roentgen-ray examination on July 13 showed that the right side of the diaphragm was much higher. It reached the level of the fourth rib at the sternal end of the fifth and ninth interspaces behind. There was a suggestion of fluid in the costophrenic

The third case was that of a girl with an abscess of the lower lobe of the right lung. In all these cases complete collapse was possible and was maintained with successful results.

In 1914 Lemann and Maes-Urban<sup>25</sup> reported a case of bronchiectasis in a colored girl aged 11, the abscess cavity being located in the lower lobe of the left lung. The lung was being kept completely collapsed at the time of the report, the patient was up and about and almost free from sputum.

In 1914, Webb and Gilbert<sup>26</sup> reported two cases of abscesses of the lung (secondary to the aspiration of a foreign body). One patient was apparently cured, the other died, probably as a result of his weakened condition.

In 1914, Zinn<sup>27</sup> described marked improvement in three patients with bronchiectasis who were treated with pneumothorax. In the first case, a man, aged 43, had bronchiectasis of the lower lobe of the left lung, complete collapse was obtained. At the time of the report two years later, the patient was without cough or symptoms and a roentgen-ray examination did not show any pathologic process in the reexpanded lung. The second case was that of a man, aged 50, who had bronchiectasis of the lower lobe of the left lung, complete collapse was maintained for months. Fifteen months after the last injection the patient was well, having no cough or symptoms. The third case was that of a woman aged 29, who had bilateral bronchiectasis, more extensive on the right side. Complete collapse of the right lung was maintained for five months, with marked improvement.

The first and second cases occurred early. The third case was an old chronic one. Zinn believed pneumothorax therapy to be a logical treatment if employed before the tissues become completely rigid.

In 1914 Matson<sup>28</sup> reported the case of a young woman with an abscess of the lower lobe of the right lung following tonsillectomy. At the time treatment was started, she was raising 500 cc of foul sputum a day. The treatment was continued for eight months, and at the time of the report she was well.

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25 Lemann, J. J., and Maes-Urban. Artificial Pneumothorax in the Treatment of Lung Abscess, *New Orleans M. & S. J.* 67:328 (Oct.) 1914.

26 Webb and Gilbert. *National Assn. Tuberculosis*, 1914.

27 Zinn, W. Ueber die Pneumothorax-Behandlung von Bronchiektasien, *Die Therapie der Gegenwart*, Berlin 16:337-344, 1914.

28 Matson, Ralph C. The Treatment of Pulmonary Tuberculosis by Means of Artificial Pneumothorax, *Northwest Med.* 6:10, 1914, *Clinical Observations on Artificial Pneumothorax with Report of Seventy-Three Cases, Discussions, Nat. Assn. Study & Prev. Tuberc.* 40:175 and 199, 1915.

ray examination did not show any evidence of air in the chest. On February 21, 700 cc of air was injected without results. On February 26, 900 cc of air was injected, on February 27, roentgen-ray examination showed evidence of air in the base of the right lung, the axillary border and the apex, but the area of pathologic process showed little collapse. On March 1, 500 cc of air was injected, and on March 3, roentgen-ray examination showed definite bands (adhesions) extending through the partially collapsed wall of the chest in the axillary margin. Mild pain was felt on the right side of the chest, but the patient did not cough so much.

On March 17, an area of almost complete dulness was felt on the right side below the level of the fifth rib posteriorly, above this region, there were increased radiance and absence of lung markings. On March 19, the chest was tapped, and purulent, thick, foul pus was found. The temperature had been rising for the last few days. On March 24, trocar thoracotomy for acute empyema was performed by Dr. Churchill. A considerable amount of foul pus was aspirated. The temperature was lower for three days and then rose again. Irrigation was performed, and there was considerable return from aspiration.

On March 29, roentgen-ray examination showed the lung distinctly collapsed with apparently complete absence of air, however, it occupied a considerably larger area than was usually seen after complete collapse. Fluid was not present. The heart was displaced to the left. On April 12, the temperature was still high, irrigation was unsatisfactory, and the patient's condition was not improving. There was epigastric pain and occasional vomiting.

On April 23, resection of the eighth rib was performed. An old sinus extending through the wall of the chest was enlarged, and a large rubber tube and two Dakin tubes were inserted into the long empyema cavity by Dr. W. Whittemore. Saline irrigations were used. On April 24, a surgical transfusion was given. On April 27, the patient felt better, vomiting had stopped and the epigastric pain was diminished. The patient was gaining perceptibly and the temperature was down to almost normal on May 2. On May 9, roentgen-ray examination showed dulness throughout the lower half of the right lung and along the axillary border to the apex. A dense shadow was seen in the lower part which was probably fluid. There was a bright area in the region of the bronchus and another just below it with indefinite lines running across. The left lung was normal.

On May 10, the temperature had risen again for a few days and on May 14 irrigation with surgical solution of chlorinated soda was started. On May 30, the patient was gaining slowly. Irrigation was continued. On June 8 a roentgen-ray examination showed that the lung was not more collapsed than before. On June 11, all of the tubes were removed and one small Dakin tube put back. On June 17, the patient was discharged from the hospital.

In January, 1924, the patient stated in a letter that she was well.

CASE 8—G. B., a white man, aged 33, Italian, married, a clipper, was admitted to the hospital on June 26, 1923. He had had intermittent pain of sixteen months' duration in the right side of the chest in the area covered by the fourth to the tenth ribs anterior to the anterior axillary line. The onset occurred with a sudden attack of pain without an initial chill or hemoptysis. The patient was in bed for two days, then resumed his work for three days, but was forced to stop on account of pain. He was then in bed for three months. His temperature varied between 102 and 103 F., and he had intermittent chills and sweats. There was no history of the inhalation of a foreign body or of an operation. Cough began with pain and did not show any relation to a change of position.



Wagner also reported the case of a girl, aged 15, who developed bronchiectasis in the lower lobe of the left lung following pneumonia and empyema. Seven insufflations were given in the course of a little more than two months. Four months after applying pneumothorax and three weeks after the last insufflation, the sputum had entirely disappeared, there was marked improvement. Later results were not known.

In 1915, Reichmann<sup>32</sup> reported the case of a woman, aged 30, with a gangrenous process involving two thirds of the lower lobe of the left lung. She was raising a large quantity of foul sputum containing elastic fibers, but tubercle bacilli were not found. The patient was given five large injections of nitrogen during eleven days, following which she made steady improvement and gained in weight. A month later she was in good condition, the cough and sputum having entirely disappeared.

Lindvall<sup>33</sup> reported the case of a woman, aged 33, who had an abscess of the upper lobe of the right lung. She raised 150 cc of foul sputum a day. She had a strongly positive Wassermann reaction and pneumothorax and injections of mercury were given from November to February, and the patient had been well for several months when the report was published.

In 1916, Dahlstedt<sup>34</sup> reported one case of bronchiectasis of long standing. The case was that of a boy, aged 13, who had had pertussis at the age of 3. Since then there had been a continual expectoration of a yellow-green sputum. The general condition of the patient was good, although there was slight cyanosis. Complete pneumothorax was obtained, the number of insufflations and duration of the treatment was not given. The patient did not come regularly for treatments.

In 1916, Cappeller<sup>35</sup> reported two cases. In the first case there was a fresh infection on one side and considerable foul sputum. Pneumothorax was maintained for one month, the cough disappeared and no more sputum was raised. Later results were not known. The condition was on one side also in the second case. The duration was unknown. Five insufflations were given in the course of fourteen days. The results were negative.

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32 Reichmann, V. Cure of Gangrenous Process of Lung by Artificial Pneumothorax, *Munchen med Wchnschr* 62 946 (July) 1914.

33 Lindvall, H. Case of Syphilitic Abscess of the Lung with Favorable Course Under Combined Pneumothorax and Mercury Treatment, *Hygiea* 77 1025, 1915.

34 Dahlstedt, H. *Nord med Ark*, 1916, no 3, vol 49.

35 Cappeller, W. Beitrag zur Pneumothorax Behandlung spezielle der Bronchiektasien und der Brustfellohlenergüsse. Inaug. diss., Jena, 1916.

Artificial pneumothorax was unsuccessful

An operation was performed on August 15 by Dr Whittemore. An incision was made for resection of the third rib and drainage of the abscess of the lung. On August 21, the condition was greatly improved, the temperature was lower, and the patient coughed less. On August 29, he was gaining rapidly; there was very little drainage, and the wound was in a satisfactory condition. On September 7 he was discharged to the outpatient department.

CASE 11—L. D., a white woman, aged 37, Jewish, married, a housewife, was admitted to the hospital on March 6, 1923. Tonsillectomy had been performed one week previously. Since that time the patient had been nauseated, had chills, a headache, and a cough with sputum, later the sputum was white and mucoid, with a foul odor. She had had a sharp, nonradiating pain in the right side of the chest for the last twenty-four hours. Her temperature varied between 99.4 and 101 F.

Examination of the chest revealed many fine to moderate crackling rales with possibly some friction rubs in the lower third of the right side of the chest extending part way into the axilla. Breath sounds tended to be bronchovesicular without a definite increase in the whispered or spoken voice. Dulness was not demonstrable on percussion. Roentgen-ray examination on March 13 showed an area of dulness on the right side of the middle part of the chest. The area was relatively circular in outline, and appeared nearer the root than the periphery of the lung, and was merged with dulness at the root. Within this area, there was a distinct area of increased radiance with an irregular convex upper border and a regular horizontal lower border. The density was much greater below than above. The symptoms were characteristic of abscess of the lung, and there was a large cavity containing fluid.

Artificial pneumothorax was instituted on March 15, 500 cc of air being injected into the postaxillary line, fourth interspace, right side, under light pressure. Free pleural oscillations were from  $-3$  to  $-1$  cm before injection,  $-2$  afterward. The patient coughed twice. Roentgen-ray examination on March 15 showed a partial collapse and a narrow area of pneumothorax in the axillary line and probably at the apex, but the immediate region of the abscess showed little collapse and a sharp and definite border.

On March 18, 500 cc of air was injected, the pressure was from  $-4$  to  $-1$  at the start and from  $-2.5$  to  $+1$  at the end. Roentgen-ray examination on March 19 showed that the right lung was a little more collapsed with air in the base along the axillary line and probably at the apex, but the immediate region of the abscess was little collapsed and showed a sharp and definite border.

On March 22, 500 cc of air was injected with difficulty because of the cough. The pressure was  $-5$  on inspiration at the start, 0 to  $+2.5$  at the end. Roentgen-ray examination on March 23 showed little compression of the lung in the region of the abscess. About one half of the space of the lung was filled with air.

On March 26, 450 cc of air was injected with ease, as the patient did not cough, with the pressure from  $-2$  to  $+1$  at the start and from 0 to  $-4$  at the end. Roentgen-ray examination on March 29 showed the lung completely surrounded by air and fairly well collapsed.

On March 31, 550 cc of air was injected with ease, as the patient did not cough. The pressure was  $-6$  at the start and  $+1$  at the end. Roentgen-ray examination on April 2 showed the right lung to be practically free from air. The cavity of the abscess was still visible and seemed a little smaller. There were bands of increased density running from the upper portion of the involved area across the chest to the axillary margin in the region of the third rib. Roentgen-ray

tuberculous lung by pyogenic organisms. After eleven injections which maintained almost complete collapse of the lung, the patient was reported as experiencing marked abatement of the foul sputum, fever and cough, and to be gaining in weight and strength.

In 1918, De Verbizier and Loiseleur<sup>42</sup> reported the successful treatment of a soldier, aged 19, who had an abscess cavity of the lung and a fluid level which resulted from influenza pneumonia. The patient was given 1,000 cc of nitrogen in two injections, obtaining a positive pressure of 4 cm. There was immediate improvement, and three weeks later, the patient was well and free from symptoms.

Weil<sup>43</sup> reported three cases of abscess of the lung. In the first case, two injections of nitrogen were given at five day intervals, and the patient was reported cured. In the second case, the patient improved, but later died of pericarditis and serous pleurisy. The third case was that of a soldier, aged 19, who had a chronic bronchiectatic cavity of the lower lobe of the right lung. A rather large amount of nitrogen was injected as follows: On September 12, he was given 500 cc, on September 14, 2,000 cc, on September 20, 2,000 cc, and on September 27, 2,400 cc. Complete collapse of the lung was obtained with the exception of adhesion at the diaphragm. The injections were unusually large to be given at such short intervals, and the patient must have had a very large pleural cavity. On December 9, the lung was completely reexpanded, the patient raising some mucopurulent sputum, but feeling well.

Bergman<sup>44</sup> treated five patients for abscess of the lung, three were cured in two months, in one patient the cavity could not be drained, and one patient died.

In 1919, Unverricht<sup>45</sup> reported seven cases of bronchiectasis, the first case was that of a woman, aged 22. Three years previously she had had pneumonia on the right side. For one and one-half years the sputum had been very foul. Seven insufflations were given in the

42 De Verbizier and Loiseleur. *Gangrene pulmonaire traitée et guérie par le pneumothorax artificiel*, Bull et mem Soc med d hôp de Paris **42** 1139, 1918.

43 Weil, P. E., and Loiseleur. *Le traitement de la gangrene pulmonaire par le pneumothorax artificiel*, Paris méd **33** 180, 1919, *La gangrene pulmonaire et ses nouvelles méthodes de traitement*, Monde med **29** 391, 1920, *Le traitement de la gangrene pulmonaire par production de pneumothorax*, Bull Acad de med, Paris **80** 393, 1918, *Le pneumothorax artificiel dans la dilatation des bronches*, Bull et mem Soc med d hôp de Paris **46** 655, 1919.

44 Bergman, H. *Für die Pneumothoraxbehandlung des Lungenabszesses*, Deutsche med Wchnschr **45** 970, 1919.

45 Unverricht, W. *Ueber Behandlung von Bronchiektasis mit künstlichem Pneumothorax*, Berl klin Wchnschr **56** 516, 1919, *Ztschr f phys u diätet Therap* **23** 393, 1919.

in the left axilla. The breath was foul. The temperature was 100 F, and the pulse rate, 98. There was slight dullness at the base of the right lung.

Examination showed a few râles when the patient coughed.

Roentgen-ray examination on March 3 showed dullness in the base of the right lung that extended more than half way across the left field, but did not reach the shadow of the diaphragm. The upper part of this area was partially obscured by the shadow of the heart and of the ribs. There was a small, rounded, relatively light area which may have represented a cavity. There was no definite fluid level. The whole appearance was suggestive of an abscess.

Roentgen-ray examination on March 15 showed the process slightly more circumscribed. A definite cavity was not made out, but there was some dilatation of the bronchial tree.

On April 30, the patient was discharged and placed in the care of a local physician. She remained in good condition for about a month, then began to be short of breath and raised a considerable amount of sputum.

On June 11 and 15, she was given 500 cc of air as an artificial pneumothorax. On June 17, there were signs of fluid in the right side of the chest, and aspiration showed a thin pus.

On June 23, she returned to the hospital. On entrance, she was breathing rapidly, and was flushed and restless. She complained of pain in the right side of the chest. Percussion over the base of the right lung elicited dullness to flatness; in this area, the breath sounds and fremitus were diminished to absent. The needle was inserted and a cloudy fluid was evacuated which had the appearance of pus. Trocar thoracotomy was performed. The patient made a fairly good convalescence, and was discharged from the hospital on August 4.

On September 6, she returned to the hospital, cough and sputum had increased. On September 8, the chest was again aspirated, but fluid was not obtained. On September 11, a resection of the rib was performed, and on September 30, the patient was discharged from the hospital with a small drainage tube in the old empyema sinus.

A follow-up note, dated August 21, stated that the tube had been removed three months before, and that the patient had been well ever since. The patient was seen on March 8, 1927. She had the appearance of a fat, healthy girl and did not have a cough or symptoms.

CASE 14—A. C., a boy, aged 11, was admitted to the hospital on Oct. 5, 1926, he had had a cough and raised sputum for six or seven months. Roentgen-ray examination showed an abscess of the upper lobe of the left lung. On October 8, 11 and 14, artificial pneumothorax was performed, 800 and 500 cc of air being injected, respectively. During the next few days the patient's temperature was higher than it had been, and signs in the chest were suggestive of fluid.

On November 8, the chest was aspirated and pus was removed. On November 9, a trocar thoracotomy was performed. On November 23 roentgen-ray examination showed capsulated fluid about the region in which the chest was previously opened. On December 10 aspiration was performed through the third inter-space axillary line, and pus was obtained. Trocar thoracotomy was performed in this region.

On December 14, the patient was discharged with pus draining from both incisions. On March 9, 1927, the patient's general condition was greatly improved, the amount of sputum had decreased and the temperature did not go above 99 F. The lower wound was closed and there was only a small amount of drainage from the upper one.

In 1922, Rist <sup>46</sup> reported ten cases of bronchiectasis. Case 1 was that of a girl, aged 5½ years. Bronchiectasis had developed in the base of the left lung following measles and bronchopneumonia two and one-half years previously. Pneumothorax therapy was given for eight months. As a result, the fever, cough and sputum quickly disappeared. Five years later the patient was cured, and remained well eight years after the end of the treatment.

In the second case, a woman, aged 34, had typical bronchiectasis. One and one-half years later pneumothorax was attempted, without beneficial results.

In the third case, a man, aged 21, developed bronchiectasis following pneumonia. Three years later pneumothorax was unsuccessful. The fourth case was that of a man, aged 29. After severe pneumonia in February, 1920, induration of the left lung developed accompanied by bronchiectasis. In September, 1921, pneumothorax was tried with partial collapse. The results were negative. The patient felt marked discomfort when the pressure was increased. The treatment was discontinued.

In the fifth case, a girl, aged 19, had had pertussis at 3½ years of age, followed by bronchiectasis. Partial pneumothorax was obtained without beneficial results.

In the sixth case, a boy, aged 9, had double bronchopneumonia following measles at 2 years of age. Since then he had had symptoms of bronchiectasis. Pneumothorax was complete.

**Summary** This was an old one-sided case in which good results were obtained.

In the seventh case, a boy, aged 13, had had pneumonia in the left lung in 1920. Bronchiectasis of the lower side of the left lung developed. Treatment by pneumothorax was given, resulting in complete collapse. In March, 1922, the patient was still under treatment.

The eighth case was that of a boy, aged 15, in whom, after influenza and pneumonia in October, 1918, bronchiectasis developed at the base of the left lung, accompanied by fever and dyspnea. In April, 1920, pneumothorax brought about complete collapse. The symptoms disappeared in a few weeks. At the time that this article was written, the patient had been working one year, and the treatment was being continued.

**Summary** This was a recent severe case with complete pneumothorax, cure was obtained.

The ninth case was that of a man, aged 24, who since childhood had had two bronchiectatic cavities of the lower lobe of the right

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<sup>46</sup> Rist, E. Un cas de bronchiectasie guérie par le pneumothorax artificiel, Bull et mem Soc med d hôp de Paris **43** 652, 1919, Le traitement des dilata-tions bronchiques par le pneumothorax artificiel, Bull med **36** 246, 1922.



Brunning <sup>51</sup> reported the case of a man, aged 38, who had an abscess of the right lung following pneumonia. He received five injections during two months, totaling 5,600 cc of air, which did not completely collapse the lung on account of adhesions. Four more injections were given, and later severe pain with dyspnea and cardiac distress occurred. The pleural cavity was aspirated, and foul smelling pus was found. Resection of ribs showed empyema accompanying gangrene of the lung. Death occurred.

Gilbert <sup>52</sup> reported three cases of abscess of the lung. Eight treatments were given in the first case, partial collapse was obtained, and further treatment was unwise. A rib resection for drainage of the abscess was performed later, followed by complete recovery.

In the second case of abscess of the lung, partial collapse was obtained with relief from symptoms. Pyothorax developed, drainage resulted in some improvement.

The third case was that of a child, aged 8, with an abscess of the lower lobe of the right lung, due to the aspiration of a tooth. Complete collapse was maintained for eight weeks. The child was reported well two months after complete reexpansion of the lung.

Dumitresco-Mante <sup>53</sup> reported a case in a patient, aged 32, who had right interlobar empyema, profuse vomiting and foul sputum. He was treated by artificial pneumothorax for four months, with marked improvement, although the sputum was still foul. He was given three doses of neoarsphenamine and 2,000 cc of nitrogen. The condition improved, and the patient began to gain weight, later, he was reported well.

Dumitresco-Mante also mentioned another case of a man, aged 30, who had interlobar empyema of the right lung. After the first injection of nitrogen, the patient began to have severe hemoptysis, fever and severe general disturbance. The injection of nitrogen was stopped. Dumitresco-Mante thought that adhesions produced an uneven collapse, blocking the exit of the pus, thus giving rise to the disturbance.

Amaudru <sup>54</sup> reported a case of a woman, aged 36, who had an abscess of the lung following a phlebitis, and was in a serious condition on account of hemorrhages and foul sputum, complete collapse was obtained.

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51 Brunning, F. *Gegen die Pneumothoraxbehandlung des Lungenabszesses*, Deutsche med Wchnschr **45** 734, 1919.

52 Gilbert, O. M. *Artificial Pneumothorax in Acute Pulmonary Abscesses*, Colorado Med **18** 138, 1920.

53 Dumitresco-Mante. *Pleuresie interlobaire traitee par le pneumothorax artificiel et neosalvarsan intraveineux*, Bull et mem Soc med d hop de Paris **44** 1215, 1920.

54 Amaudru, J. *Plebite variequeuse, embolies, Abscess du poumon consecutive, guerison rapide par le pneumothorax therapeutique*, Bull et mem Soc. med d hôp de Paris **44** 1380, 1920.

CASE 20—L M, a white man, aged 25, Irish, single, a messenger was admitted to the hospital on May 15, 1923. Five years previously he had had influenza, pneumonia and pleurisy and had been in bed almost all winter. Since then the cough and the sputum had gradually increased. The sputum was greenish yellow, a cup full was expectorated in the morning, but it was never bloody or particularly foul. The patient had infantile paralysis at the age of 12 or 13 years, and this condition remained for fifteen years. He had a disease of the stomach for nine years.

Examination revealed a pathologic process in both lungs. The fingers were clubbed, and the patient was cyanotic. Roentgen-ray examination on May 16 showed increased density in the region of the left descending bronchus and the outline of bronchi mottled with a suggestion of dilatation of small bronchi. On the right side, there was increased density about the hilum and general peribronchial thickening. The appearance suggested bronchiectasis. The apices and the periphery of the lungs were normal. Roentgen-ray examination on May 17 also showed many bronchiopneumonic patches scattered through both lungs with one large area in the upper left side of the chest. The areas were most dense in the center and gradually faded toward the periphery.

Artificial pneumothorax was attempted on May 20, but a pleural space was not found. On May 21, 150 cc of air was injected into the left anterior axillary line, in the sixth space, with a pressure of +4. On May 22, roentgen-ray examination showed a small gas bubble above the diaphragm on the left side; otherwise there was no evidence of air. On May 23, roentgen-ray examination and the high pressure which resulted from a small injection of air indicated that probably there was no pleural space. As the patient was in poor condition and as the process was bilateral, treatment was discontinued.

CASE 20—M R, a white man, aged 50, a Russian teamster, a widower, was admitted to the hospital on June 20, 1923. He gave a history of persistent cough for many years. Two years previously he had had several teeth removed under ether anesthesia. Shortly afterward the symptoms increased: he raised sputum, but not in an excessive amount. Two months after the extraction, he missed a tooth from his plate, but did not think that he had swallowed it. In March, three and a half months before admission he had a sudden attack of pain, the sputum increased greatly and became foul.

Examination of the chest revealed a localized process at the base of the left lung showing slight dulness. Tactile and voice fremitus were diminished and respiratory movements were much diminished. Moderate coarse moist inspiratory rales were heard. The nails were clubbed. Roentgen-ray examination revealed a pathologic process at the root of the left lung which involved the surrounding structure of the lung and which interfered with the passage of air. Encapsulated empyema and bronchiectasis would not account for the entire picture. The condition might have been abscess of the lung; a chronic disease of the lung should be considered.

Artificial pneumothorax was performed on June 28. 400 cc of air were injected into the left side. On June 30 roentgen-ray examination showed a suggestion of a small amount of air in the extreme apex of the left lung. Air was seen in the subcutaneous tissues in the left side of the chest. The collapse was noted.

On July 3 700 cc of air was easily injected. Roentgen-ray examination on July 6 still showed a small amount of air in the apex of the left lung, but no further collapse. On July 7 air was injected. There was considerable subcutaneous emphysema. Subjectively the patient was much better. He was



Rich<sup>60</sup> (1922) reported some interesting results in ten cases of acute abscesses of the lung

A patient with an abscess of the upper lobe of the right lung was treated for twelve days with four small injections of air, totaling 900 cc. He was reported well and free from symptoms six months later

Another case was that of a man, aged 48, who had an abscess of the upper lobe of the right lung, or an interlobar empyema. He was given 275 cc of air, and a large amount of pus was evacuated at once. A second attempt to give air caused a slight pleural shock, so gas was not given. The patient left the hospital two weeks later, free from symptoms

In another case of abscess of the lung following appendectomy, the patient improved after the injection of 350 cc of air, he then died of asthenia

In a fourth case, the patient had an abscess of the lower lobe of the right lung, or an interlobar empyema. He was given 550 cc of air, a large amount of pus was expectorated, and a second injection was given seven days later. The patient was reported well

In cases 7, 8 and 10, pneumothorax resulted in partial collapse with improvement

Two patients recovered spontaneously

In one case, pneumothorax was impossible, and surgical drainage was followed by death

In 1921, Ribara<sup>61</sup> reported the case of a young man who developed a bronchiectatic cavity with a diameter of 10 cm after influenzal bronchopneumonia. Marked improvement resulted after pneumothorax therapy (duration and amount not given). Later results were not known

Singer<sup>62</sup> reported the case of a patient with a bronchiectasis of two years' duration, who was raising a quart of pus a day. Following three severe hemorrhages, the lung was collapsed. The patient did not have further trouble

Singer and Graham<sup>63</sup> reported two cases of bronchiectasis of several years' duration. One patient was a boy, aged 17, partial pneumothorax brought some relief. The cavity in the lower lobe was not collapsed. Lobectomy was performed, and the patient recovered

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60 Rich, H. M. Acute Lung Abscess Treated by Therapeutic Pneumothorax, *Am J M Sc* **164** 428, 1922

61 Ribara, A. *Bol d clin*, 1921, no 7, vol 38, Ref I *Zentralbl f The forsch* **16** 559, 1922

62 Singer, J. J. Pneumothorax in Tuberculosis and Bronchiectasis, *J Missouri M A* **19** 89, 1922

63 Singer, J. J., and Graham, E. A. The Newer Treatment of Bronchiectasis, *J Missouri M A* **19** 390 (Sept) 1922

pleural cavity contained a considerable amount of air and pus. On January 28 sections of the upper six ribs were removed under gas-oxygen anesthesia. On February 2, the patient died.

CASE 22—P. M., a girl, aged 17, was admitted to the hospital on Aug. 6, 1926, with a diagnosis of bronchiectasis of the lower lobe of the left lung following what was probably bronchial pneumonia seventeen months before. She had a cough and raised from between 8 to 12 ounces (236 to 355 cc.) of purulent sputum. On August 8, roentgen-ray examination showed a dull area in the lower portion of the left side of the chest. The dullness was of a mottled character, extending up along the crest of the bronchial tree. The diaphragm was high on this side. The intercostal spaces were narrow. The heart and mediastinal contents were displaced to the left. The appearance was that of a chronic destructive process involving the lower lobe of the left lung.

On August 24, bronchoscopy was performed and iodized oil 40 per cent was injected. A roentgen-ray examination showed many discrete cavities in the lung tissue filled with the oil.

On September 6, artificial pneumothorax was given, 600 cc. of air being injected. On August 8, 600 cc. of air was injected, on August 12, 800 cc., and on August 20, 400 cc. Roentgen-ray examination on October 2 showed that the lung was completely collapsed. On October 25, the patient was discharged. Artificial pneumothorax was continued after the patient left the hospital.

On Feb. 24, 1927, bronchoscopy was performed. A small amount of pus was aspirated from the bronchus going to the lower lobe of the left lung. There was no evidence of collapse of the bronchi.

The patient said that she raises about 1 ounce (30 cc.) of sputum a day. She is in good physical condition. The lung is still collapsed.

In 1903, Riva-Rocci<sup>1</sup> reported the successful result of pneumothorax therapy in two cases. The first case was that of a boy, aged 11, who had an extensive bronchiectasis of the right lung of four years' duration. The second case was that of a man, aged 28, who had an abscess of the upper lobe of the right lung of three months' duration, while under observation, he developed a valvular pneumothorax which nearly proved fatal. He was successfully treated by injecting nitrogen into the pleural cavity, collapsing the lung.

In 1908, Brauer<sup>2</sup> reported four cases of bronchiectasis in which the patients had the disease many years, three of whom improved after the treatment by pneumothorax.

One case was that of a girl, aged 16, who had bronchiectasis on both sides. She had been ill three years, and had fever and hemorrhages. In the course of twenty days three insufflations were performed, which gave a definite but partial pneumothorax. There was a slight exudate. Three weeks later thoracotomy was performed, with resection of a rib and loosening of several strong adhesions. The

1 Riva-Rocci: *The Therapeutic Application of Artificial Pneumothorax*. *Gaz. med. ital.*, no. 27, July 2, 1903, p. 261.

2 Brauer: *Die therapeutische Bedeutung des künstlichen Pneumothorax*. *Klin. therap. Wchnschr.*, July, 1908, no. 28, p. 794.

injections were followed by hemoptysis and discontinued, surgical drainage afforded relief, but was attended by a persistent sinus

The second patient developed empyema twenty-four days after collapse had been induced. He died a month later after developing signs of pneumothorax on the untreated side

Pelle<sup>69</sup> reported the case of a patient with an interlobar empyema, who was cured after five months' treatment with artificial pneumothorax

By four injections of air, Troisier and Gayet<sup>70</sup> completely cured a patient with postpneumonic interlobar empyema communicating with a bronchus. The expectoration disappeared completely, and the temperature fell to normal after the second insufflation

Perkins and Burrell<sup>71</sup> cited seven cases of abscess of the lung and six cases of bronchiectasis to show the value of artificial pneumothorax in these conditions. Three patients with abscess were completely cured after treatment was continued from five to fourteen months. Two cases were complicated by rupture into the pleural cavity, one four days and the other three months after the institution of treatment, however, both patients made a complete recovery after drainage. One patient showed improvement in the general condition with a reduction of sputum, and complete recovery followed a thoracoplasty performed because of adhesions. In the remaining case, the collapse was incomplete because of adhesions, but the sputum was reduced from 7 to 2 ounces (from 207 to 59.2 cc). Death followed surgical drainage

Of the six patients with bronchiectasis, one is reported cured, two have shown marked improvement and are still under treatment, two showed a temporary improvement, but died following thoracoplasty performed because of adhesions, the condition of one patient with a bilateral case did not show any noteworthy change following successive collapses of the two sides

Harrell<sup>72</sup> treated an extremely ill patient by collapse during a period of thirteen weeks. At the end of a year, she was afebrile and in good condition, except for slight cough and some persistent expectoration. Harrell believed that in "all cases of pulmonary abscess, especially in extremely ill patients, pneumothorax should be given or tried before more radical procedures"

69 Pelle, M. A. Pneumothorax thérapeutique au cours d'une pleurésie interlobaire, *Bull et mem Soc med d hóp de Paris* 47 754, 1923

70 Troisier and Gayet. La cure de la pleurésie interlobaire et des suppurations pulmonaires par le pneumothorax thérapeutique, *Bull et mem Soc. med d hóp de Paris* 47 867, 1923

71 Perkins and Burrell. Artificial Pneumothorax. Its Application to Cases Other Than Those of Pulmonary Tuberculosis, *Lancet* 1 478 (March 10) 1923

72 Harrell, C. L. Report of a Case of Pulmonary Abscess of Lower Lobe Treated by Artificial Pneumothorax, *Virginia M Monthly* 49 585, 1923

In case 1 the condition was chiefly on one side and of several years duration. Application of pneumothorax was not successful.

In the second case, the condition was chiefly on one side. The patient had been ill for many years. Pneumothorax was not successful.

In the third case, also, the condition was chiefly on one side. The duration of the illness was not given. Only one insufflation was given and the patient did not return for further treatment. The results were negative.

In the fourth case, both sides of a patient, aged 18, were affected. The duration of illness was not known. There was alternating pneumothorax during two or three weeks. Several months later three insufflations were given on the left side. After two and three-fourths months the left lung entirely collapsed and the râles disappeared but the sputum remained unchanged. One month after treatment, the lung was re-expanded and râles were heard again. This was probably an advanced case. Despite complete collapse of the lung the results were negative.

In 1910, Forlanini<sup>4</sup> reported a case of abscess of the lung in a woman, aged 24, who was cured. The abscess followed a croupous pneumonia and was of six years' duration. The patient was under treatment for fifteen months in 1904 and 1905 and when the case was reported, she had been in excellent condition for four years having a fully re-expanded lung.

Forlanini mentioned that he successfully treated one patient with bronchiectasis. Later reports were not given.

In 1910, Oscar Frank and von Jagic<sup>5</sup> reported the case of a patient, aged 28, with a double infection. Internal treatment for more than one year was unsuccessful. The patient was cyanotic and slightly dyspneic. He had clubbed fingers. Five insufflations were given in one month, and a large but only partial pneumothorax of the right side was obtained. The condition improved considerably, the dyspnea disappeared. There was marked improvement in the clubbed fingers. The râles practically disappeared and the cavities distinctly decreased in size. The patient was still under treatment when the report of the case was published.

**Summary.** Despite the short treatment with only partial pneumothorax, in this case of double infection which probably was not of long standing decided improvement was noted. The subsequent history is not known.

4 Forlanini C. Lung Abscess of Six Years Duration Successfully Cured by Artificial Pneumothorax. *Gaz med ital* March 10-17, 1910 no. 10 11 p. 41.

5 Frank and Jagic. Ueber Pneumothoraxtherapie bei Bronch. *Wien klin Wchnschr* 1910 no. 21 p. 771.

1919, with a diagnosis of postpneumonia and nontuberculous induration of the lung with bronchiectasis. On May 23, artificial pneumothorax was applied to the right side. At the second insufflation, 500 cc could be given. Nineteen insufflations were given, the last on December 16. Only partial pneumothorax was obtained. The hemorrhages stopped. The sputum and cough decreased. On December 31, there was a sudden rise of temperature. Râles appeared at the bases of both lungs, and after continued high temperature, the patient died on Jan 2, 1920. Autopsy showed a bronchopneumonic area in the center of the lobe of the left lung, a slight amount of exudate was present in the cavities, but there was no evidence of tubercle bacilli.

The fifth case was that of a woman, aged 20. In June, 1920, pain developed in the right side of the chest, but there was no fever. In August, she coughed up a tablespoonful of blood. The sputum was foul. On Nov. 10, 1920, she entered a sanatorium. On December 2, pneumothorax was applied and continued until Oct 29, 1921, twenty-seven insufflations being given. Only a partial pneumothorax was obtained. Despite this there was an apparent, temporary improvement with a normal temperature after the eighth insufflation, and a decrease of sputum resulted. The general condition of the patient improved. Hemorrhage did not occur during the last six months of treatment.

By February, 1921, the râles had disappeared. From that time on, the pneumothorax cavity gradually decreased in size, and less and less gas was used. At the same time, the râles returned in the partially collapsed lung. Râles also appeared at the base of the lung (left), and club fingers developed. Treatment was interrupted. The patient died at home in November, 1922.

In the last two cases, the condition was more advanced than in those previously mentioned, only a partial pneumothorax could be obtained, because of the tight band of adhesions and the fact that the condition was a double one.

Tewksbury<sup>74</sup> said that since 1917 he had seen fifteen patients who were treated medically, 25 per cent recovered, the condition became chronic in 5 per cent, and 40 per cent died within a three year period. Surgical methods give a high percentage of recoveries, but convalescence is slow. Of thirty-five patients with acute abscess who were treated by pneumothorax, Tewksbury reported a prompt recovery in twenty-eight cases (80 per cent). In three cases, the abscess ruptured into the pleura, and drainage was instituted through the wall of the chest. Complete cure resulted within a few months. Four patients died. Usually only six or seven treatments were necessary.

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<sup>74</sup> Tewksbury, W. D. Acute Pulmonary Abscess Following Tonsillectomy, Treated with Artificial Pneumothorax, *Ann Clin Med* 4 347, 1925.

In 1912, Koniger<sup>9</sup> reported two cases of bilateral chronic bronchiectasis in which the patients were treated by artificial pneumothorax. After a relatively short time, the treatment did not give satisfactory results. In one case, however, the amount of sputum was reduced from 50 to 60 cc to from 10 to 30 cc, in the other from 180 cc to 20 cc.

Wagner, in a communication to Professor Koniger, reported two cases of bronchiectasis. The first case was that of a woman aged 23 who had bronchiectasis of the lower lobe of the left lung following pneumoma and abscess of the lung. Artificial pneumothorax in three injections of 1 liter each was given in six weeks. The sputum was reduced from 70 cc to 30 cc, the patient improved daily and was able to work. Two months after the application of artificial pneumothorax the lung expanded to three fourths of its size.

In the second case, a girl aged 15, had bronchiectasis of the lower lobe of the left lung following pneumonia and empyema. She raised 100 cc of foul sputum a day. Artificial pneumothorax in seven doses of from 400 to 700 cc of nitrogen was given in less than three months. A pleural effusion developed. Four months after the beginning of artificial pneumothorax and three weeks after that there was marked improvement. Three months later, the sputum had disappeared entirely.

In 1912, Lowenhjelm<sup>10</sup> reported the case of a woman aged 30 who had an abscess of the middle lobe of the right lung of six years' duration, which was caused by the aspiration of a capsule of resinoid. The patient raised from 350 to 500 cc of foul sputum a day. The sputum contained many elastic fibers, on repeated examination tubercle bacilli were not found. She was given an intensive treatment of colloidal silver intravenously which was followed by great improvement. She married and had a child. In 1911, on account of a recurrence of the old symptoms she was given treatment by artificial pneumothorax.

From Oct. 11, 1911, to Nov. 4, 1911, she received seven injections of nitrogen—250, 500, 400, 300, 500, 800 and 500 cc respectively. Good compression was obtained above and below the abscess which was adherent to the wall of the chest. Adhesions prevented the collapse of the abscess which was the size of a closed fist. The expectoration diminished at first, but after a short time continued as before. She gradually grew worse and dyspnea increased, with loss of strength and rise in temperature.

9 Koniger. Ueber die Technik und Indikation des kunstlichen Pneumothorax. *Therap. Monatsh.* 26: 851, 1912.

10 Lowenhjelm, Carl. Ett fall af kavernbildning i lungan efter bukaltersabscess behandlad med pneumothorax artificialis. *Hygien* 74: 992, 1912.

Heuer and MacCready<sup>81</sup> mentioned five cases in which the patients were treated by artificial pneumothorax after exploratory thoracotomy. Two patients were well for from one to ten or more years, the other three could not be traced, but they had recovered at the time treatment was discontinued.

According to Whittemore,<sup>82</sup> from 10 to 30 per cent of the patients may be expected to be cured by expectant treatment. Artificial pneumothorax may cure a small number, it should be used only in those cases in which the lung and costal pleura are not adherent. It is an excellent means of determining whether or not adhesions are present. Bronchoscopy may cure a limited number of patients if treatment is established early. Surgical measures offer an excellent chance for cure in those cases in which other methods have failed or are unsuitable. In eighty-six of the author's cases, 10 per cent of the patients recovered with expectant treatment. In fifty-two cases in which surgical measures were used, the mortality was 15 per cent.

In 1924, Meyer-Bornecke<sup>83</sup> reported eleven cases in which artificial pneumothorax was used. Three of the patients died, one was discharged unrelieved, one improved and six were cured. Two of the three patients died who had cases that were not suitable for the employment of pneumothorax, as the process was gangrenous. In the second case, pneumothorax was not applied until the day before death. Of the six patients who were cured, four had gangrene, one an abscess of the lung, and the other had a putrid abscess.

In 1925, Winner<sup>84</sup> reported five cases. In the first case, the patient had an abscess of the lower lobe of the left lung following tonsillectomy. There was slight improvement following postural treatment, but as the temperature was intermittent, pneumothorax was started, twelve installations of gas being given. The patient recovered.

In the second case, an abscess developed in the lower lobe of the right lung following appendectomy. The patient had chills and fever. From three to four cups of foul sputum were expectorated daily for one month. Pneumothorax treatment was given for seven weeks, the patient received in all 6,500 cc of gas, and recovered.

In the third case, the patient had an abscess in the middle lobe of the right lung following influenza. He raised a large amount of foul

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81 Heuer and MacCready. Lung Abscess, *Arch Surg* 6:337 (Jan) 1923.

82 Whittemore, W. Etiology and Treatment of Nontuberculous Abscess, *Surg Gynec Obst* 38:461, 1924.

83 Meyer-Bornecke. Ueber die Behandlung von Lungengangrän und Lungenabszess, mit besonderer Berücksichtigung der Pneumothoraxtherapie, *Mitt a d Grenzgeb d Med u Chir* 37:65, 1923.

84 Winner, P. S. A Study of Twenty-Two Cases of Lung Abscess, *Illinois M J* 47:267, 1925.

flations was not published, because he was still under treatment at the time the article was published. The lung collapsed to the size of a small hand, with a few bands of adhesions on the front side of the thorax.

The patient was able to do full time work and was almost entirely free from symptoms. If there was too long an interval between the insufflations, the sputum and cough returned.

**Summary.** In a double postpneumonic process with free pleural space, an almost complete pneumothorax was produced in the more involved lung, and as long as insufflations were repeated frequently enough, the sputum was kept in abeyance with good effect. Subsequent results were not known.

In 1912, Brauns<sup>12</sup> reported three cases of bronchiectasis. The first occurred in a woman, aged 27, with the process on one side. Twelve insufflations were given. The patient was cured, although no later reports were given.

The second case was that of a man, aged 41, with a one-sided process. Seventeen insufflations were given. The patient was cured. Later examinations were not made.

The third case was that of a man, aged 40. There were changes in both lungs. He improved after seventeen insufflations and was still being treated at the time the article was published.

In 1913, Penzoldt<sup>13</sup> reported that in one case improvement did not appear until long after pneumothorax. The patient then grew worse owing to a pleural infection. After immediate thoracotomy was performed and extensive treatment of the pleura was given, complete cure resulted. A later report was not given.

PekanoVIC<sup>14</sup> gave a brief abstract of one case in which only partial pneumothorax was obtained, owing to pleural adhesions, but temporary improvement was noted in the hemorrhages as well as in the temperature.

In 1913, King and Mills<sup>15</sup> reported unsuccessful treatment of a man with an abscess of the lung and infection of the sphenoidal sinuses. After three injections of nitrogen (500, 600 and 600 cc. respectively) the treatment was discontinued. Improvement was not noted and the patient died two weeks after discharge from the hospital.

In 1913, Izar<sup>16</sup> reported the case of a man, aged 55, with an abscess of the upper lobe of the right lung, who was treated with

12 Brauns, H. *Ztschr. f. Tuberk.* **18**: 549, 1911-1912.

13 Penzoldt. *Verhandl. d. Kongr. inn. Med.* 1913, p. 25.

14 PekanoVIC, S. *Budapesti orv. t. g.* 1912, 10: 57. *Internat. J. Tuberc. Forsch.* 1912-1913, p. 74, 1917.

15 King and Mills. *Am. J. M. Sc.* 1913, 10: 173, 1913.

16 Izar, G. *Un caso di ascesso polmonare con empiema e pneumotorace artificiale.* *Policlinico* **20**: 449, 1917.



cold which was followed by cough. He expectorated mucopurulent sputum which became purulent and gradually increased in amount, until he was spitting about a sputum box full a day. This persisted for some time, and gradually the condition improved, but each time he developed a cold or an infection of the upper respiratory tract, it would be followed by expectoration of quantities of sputum which at times had a foul odor. About a year before this article was written, he had a severe pleuritic pain in the right side of the chest. During these years of frequent invalidism, he gradually lost weight. The sputum was examined many times, but did not show any tubercle bacilli. On admission, there was a dense homogeneous shadow at the base of the right lung, and the physical signs showed consolidation with cavity formation.

His fingers were markedly clubbed, and there was a strong odor to his sputum on admission to the hospital, he did not have fever.

About a month after admission, a bronchoscope was passed down into this cavity, the pus evacuated and iodized oil 40 per cent inserted.

Pneumothorax or artificial collapse of the lung was begun on Nov. 23, 1926. Within six weeks after the collapse was started, he became free from symptoms and has remained free for four and one-half months, the time of the last report.

Since admission, he had gained in weight from 110 to 144 pounds (49.9 to 65.3 Kg.).

abscess was caused by the inhalation of a small bone twenty months previously. She raised from 750 to 800 cc of foul sputum daily. She was treated for nine months, and following the last injection of 1,080 cc of nitrogen, she had a severe coughing spell, during which she expelled a small piece of bone. Seven months after the last injection, the patient was in excellent health, she had only a slight cough and raised only 1 ounce (30 cc) of sputum daily.

In 1914, Nugel<sup>22</sup> reported the case of a youth, aged 17, who had been ill a long time. The left half of the chest was narrower than the right. Nine insufflations were given in two and one-half months and there was complete pneumothorax. Less than four months after the treatment was begun, the patient's general condition was good, there was little sputum and it was not foul. The patient was relatively cured. Later results were not given.

**Summary.** This was an old, principally one-sided process without marked physical signs or adhesions. Complete pneumothorax quickly brought about a cure, but the sputum did not disappear entirely.

In 1914, Jacobaeus<sup>23</sup> reported a case of a man, aged 34 who had been coughing at times for the past fourteen years. During the last four years, there had often been blood in the sputum. Attempts at pneumothorax were ineffectual, and for nine months, insufflations were given anteriorly and a diffuse pneumothorax developed over the upper lobe. The patient had difficulty in expectorating a large amount of sputum. Septic symptoms appeared and the patient died.

**Summary.** This was a one-sided advanced case of double synchia of long standing. Partial pneumothorax brought about collapse of one healthy lobe and sepsis.

Leuret and Aubert<sup>24</sup> reported three cases in which treatment was successful. The first case was that of a man who had an abscess of the middle lobe of the right lung of two years' duration. He raised large quantities of sputum and had had a severe hemorrhage. The second case was that of a boy with an abscess of the middle lobe communicating with a bronchus who also had had a severe hemorrhage.

22 Nugel. Zur Kasuistik des künstlichen Pneumothorax bei Tuberkulose und Bronchiektasien. Inaug. diss. Jena 1914.

23 Jacobaeus, H. C. Nord. med. Ark. 1914, nos. 1-4 vol. 47.

24 Leuret and Aubert. Un cas d'abcès du poulmon ou de bronchie dans les bronches guéri par le pneumothorax artificiel. Gaz. heb. de Bordeaux, June, 1914, no. 26, p. 303. Second observation de pneumothorax artificiel. Ibid., June 1914, no. 26, p. 305. Un cas d'abcès de l'interlobe évacué dans les bronches guéri par le pneumothorax artificiel. med. de Paris 86 71 1915.

off drainage already partially established, resulting in an exacerbation rather than a relief of symptoms. This has been our experience in some cases and has been reported also by others. We also feel that the expulsive action of the cough, which is, after all, the one most important factor in lung drainage, may be hampered in a lung partially immobilized by a pneumothorax.

Our most serious objection, however, is the very real danger that the pleura may be ruptured when this method is employed in abscesses, with a resulting acute septic empyema necessitating immediate operation and under circumstances which render the danger to life exceedingly great. We have had a few such experiences and reports of similar cases occur rather frequently in the literature.

Upon the whole, therefore, we believe that this procedure carries with it too great a risk to warrant its employment as a routine procedure in the treatment of lung abscess at the same time realizing that with a fortunate combination of circumstances, especially in lesions situated near the hilum, brilliant results, as in one of our own cases, may be obtained by its use.

We have consequently employed artificial pneumothorax in only ten cases out of one hundred which we recently gathered together for study and in one of these prompt recovery ensued. In the others it seemed to have little or no effect.

Whittemore<sup>3</sup> has expressed himself repeatedly on this subject, and in his latest publication he said that artificial pneumothorax will cure a limited number of patients, especially if it is instituted early. Little can be accomplished if this is not undertaken until the lung and the costal pleura are adherent, therefore a collapse of the lung must be brought about early, before this takes place. In certain instances in which there are firm adhesions, a partial collapse of the lung may be of temporary benefit. This procedure, by diminishing the distressing cough and the foul odor of the sputum, so that the patient obtains rest and nourishment, may improve the condition of the patient so that operation may be performed. A careful search of the literature has failed to reveal any considerable number of patients cured by this method. Once in a lifetime there is a "freak" case in which the patient has been cured by one injection of air. We have had one such case. The danger of tearing an adhesion, and thereby opening an abscess situated in the periphery of the lung and producing an empyema, should be remembered.

Tewksbury<sup>4</sup> is the most enthusiastic advocate of this method of treatment. In several articles he reported a high percentage of cures.

Lockwood<sup>5</sup> said that artificial pneumothorax should be tried for the small encapsulated abscess not connected with a bronchus, and perhaps for the ordinary long-standing, well localized abscess.

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3 Whittemore, Wyman. *Boston M & S J* **192** 664 (April) 1925

4 Tewksbury, W. D. *Pulmonary Abscess, J A M A* **68** 770 (March 10) 1917, *Pneumothorax in Nontuberculous Lung Abscess, ibid* **70** 293 (Feb 2) 1918

5 Lockwood, A. L. *Lung Abscess, Arch Surg* **6** 314 (Jan) 1923

Matson also reported successful treatment in a case of postpneumonic empyema in which he aspirated the pus and injected nitrogen to maintain the lung in a state of collapse.

In two cases of bronchiectasis, collapse was not possible owing to extensive adhesions. A case of abscess of the lung in a diabetic person and a case of gangrene of the lung is reported in which lasting benefit was not obtained from collapse therapy.

In 1914, Balboni<sup>29</sup> reported a case of abscess of the upper lobe of the right lung and a case of bronchiectasis of the left lung in which the patients were successfully treated by artificial pneumothorax. They were well and free from symptoms one and two years respectively after suspension of treatment.

Balboni also reported the case of a man, aged 50 with an abscess of the lower lobe of the left lung, in which treatment by artificial pneumothorax was attempted because the condition of the patient did not permit a surgical operation. Only a partial pneumothorax was possible as the lower lobe was adherent, and treatment had to be discontinued. There was some symptomatic relief, because further injections caused cardiac distress, severe dyspnea and coughing, treatment was abandoned.

In the case of diffuse bronchiectasis of the right lung with a lesser involvement of the lower lobe of the left lung symptomatic relief was obtained. Ten months after the suspension of the pneumothorax the lower lobe of the right lung was drained surgically by Dr. Wynn Whittemore. These are cases 21, 22, 53 and 59 of the series.

In 1914, Zink<sup>30</sup> reported among his 110 cases the following case of bronchiectasis. A boy, aged 9, had been ill for three years with a bronchiectasis in the lower lobe of the left lung and had expectorated a large quantity of sputum which did not show tubercle bacilli. He was treated from April 1912, to February 1913, during which period his general condition was good, the sputum diminished in quantity but remained fetid. Despite the youthful age of the patient Zink felt that it is questionable whether a cure could be effected by pneumothorax.

In 1915, Wagner<sup>31</sup> reported the case of a man, aged 28, who had bronchiectasis of the lower lobe of the left lung following pneumonia. Three insufflations were given in the course of six weeks. There was marked improvement, the patient being able to do full time work. Ten months after pneumothorax was applied the lung had stretched out to three fourths of its volume. Nothing was known of the later results.

<sup>29</sup> Balboni, G. M. *Forlunius Artificial Pneumothorax—A Study*. Ed. 1. Paris, Boston, M. & S. L. **171** 697 (Nov. 5), 1914. **171** 955 (Dec. 24), 1914. A discussion on abscess of the lung and bronchiectasis. *Tr. Am. Soc. S. C.* **22** 619, 1914.

<sup>30</sup> Zink. 110 Fälle von künstlichem Pneumothorax und deren Beobachtungen. *Beitr. z. klin. d. Tuberk.* **28** 155, 1914.

<sup>31</sup> Wagner. *Diss. Erlang.* 1915.

from 3 to 4 ounces of thin, foul pus as if an abscess had ruptured. A roentgenogram taken immediately after the evacuation showed far less density than before, and it was possible to demonstrate many small cavities. In addition, there was a suspicion of a pleuritic effusion.

The child continued to fail, however, and more radical measures were considered. An exploratory puncture was made in the eighth intercostal space chiefly to determine whether an empyema existed. About 1 cc of the same foul pus was found that was being expectorated, but it could not be determined whether it had been obtained from the pleural cavity or from the lung. Immediate

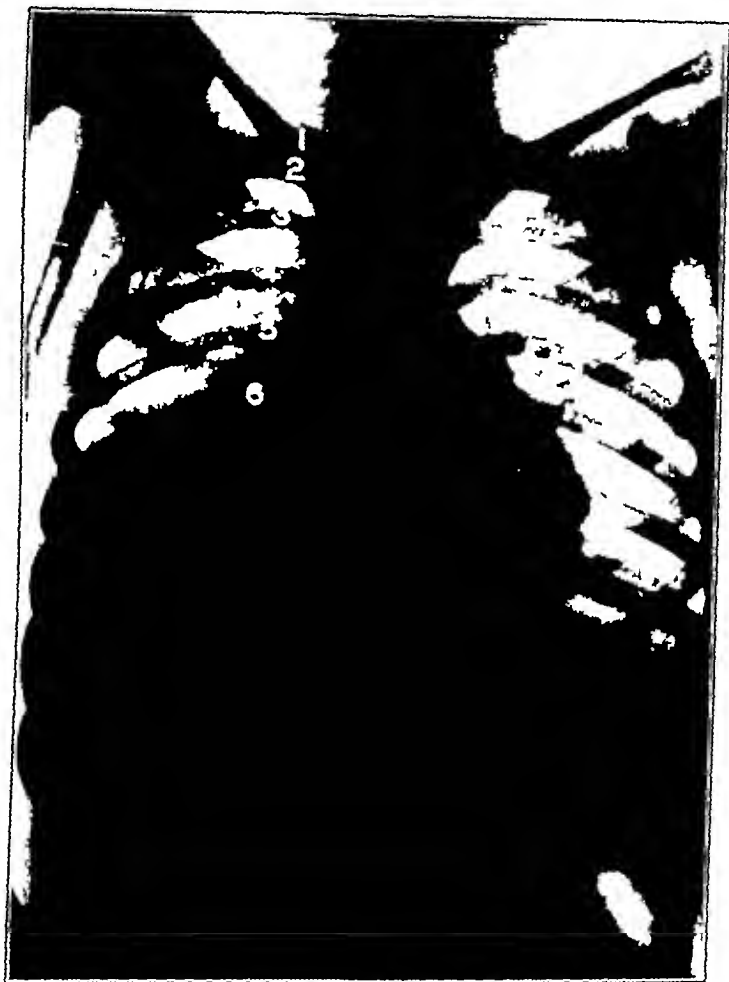


Fig. 1—Suppurative involvement of lower right lobe extending to level of sixth rib

operation was advised and carried out the same day. Under local anesthesia, about two inches (5 cm) of the ninth rib was resected in the posterior axillary line. Repeated punctures through the rib bed were negative. Air rushed into the pleural cavity through these punctures, and the attempt to strike pus was abandoned. A small safety-pin was placed against the parietal pleura at the site of the original puncture, to be used as a future guide, and iodoform gauze was then packed into the wound to favor pleural adhesions, the intention being to institute drainage at a later operation. With the exception of marked cyanosis, the child stood the operation well and did not show unusual signs of shock or dyspnea. A roentgenogram was taken at once that showed partial collapse of the

In 1916, Epifano<sup>36</sup> reported the case of a man aged 57 with abscess of the lower lobe of the left lung communicating with a bronchus. He was treated for four months and recovered.

In 1916, Antonucci<sup>37</sup> reported the case of a woman aged 59 with an abscess of the middle lobe of the right lung communicating with a bronchus. The patient was treated for four months. Good collapse was obtained in spite of an adhesion of the upper lobe. The patient was well several months after complete reexpansion of the lung.

Antonucci also made note of a case of pulmonary gangrene following an acute condition resulting from a perforated appendix. In this case artificial pneumothorax acted unfavorably because the collapse obtained interfered with the emptying of the abscess cavity.

Greer<sup>38</sup> reported a case of a boy, aged 5 who had an acute interlobar empyema which was draining through a bronchus. Three injections of nitrogen were given from May to June. The pus entirely disappeared, and four months later, the lung reexpanded. The child was reported in perfect health.

In 1917, Tewksbury<sup>39</sup> reported two cases of abscess of the lung in which the patients were treated by artificial pneumothorax. In 1918, he reported ten cases and in 1919, he gave a final report of fourteen cases, in eleven of which recovery was reported one and two years after the suspension of treatment. He concluded by saying that artificial pneumothorax used early is the most rational and successful treatment for abscess of the lung.

Klinkert<sup>40</sup> reported a case of chronic abscess of the lung of six months' duration, with fever, loss of weight and foul sputum. The patient was given thirteen injections during three months. Three months after the last injection, he was reported well.

In 1918, Simons and Swezy<sup>41</sup> reported a case of acute pulmonary abscess in a woman aged 22, due to secondary invasion of a chronically

36 Epifano G. Un caso di gangrena polmonare guarita col pleurismo artificiale, *Ann di clin med* 7 25, 1916.

37 Antonucci, C. Un caso di gangrena polmonare acuta e recidivata curata con il pneumotorace artificiale alla Forlanini. *Riv osp* 6 745, 1916.

38 Greer A. E. Interlobar Empyema Treated by Artificial Pneumothorax. *J A M A* 66 1019 (April 1) 1916.

39 Tewksbury W. D. Acute Pulmonary Abscess Treated with Artificial Pneumothorax. Two Cases. *J A M A* 68 770 (March 10) 1917. Treatment of Nontuberculous Lung Abscess with Pneumothorax. Report of Ten Cases. *ibid* 70 293 (Feb 2) 1918. Acute Pulmonary Abscess. Report of Four Cases Treated with Artificial Pneumothorax. *New York M J* 110 840, 1919.

40 Klinkert. Pneumothorax en dorstkwabehandeling bij pleuritis. *Geneesk Nedel Tijdschr v Geneesk* 3 67, 1918.

41 Simons and Swezy. An Acute Pulmonary Abscess Treated with Artificial Pneumothorax. *Am Rev Tuberc* 2 92, 1918.

formed to prove this, and iodized oil 40 per cent was injected into the lower lobe, with the result shown in figure 4. A contracted little lobe with dilated bronchi was outlined. This lobe has remained in the same state and has not given rise to symptoms. The other lobes completely fill the chest, as shown in figure 5, which was taken eight months after operation. The patient has remained well.

#### COMMENT

What does such a case teach? Is it simply one of the freak cases of which Whittemore speaks, or does it point the way to better understanding and treatment in certain well selected cases? We were dealing



Fig. 3.—Pneumothorax on the right side and partial collapse of all lobes one week after operation.

with a pus-soaked lung with a good bronchial outlet, no other method of treatment would have been as effective. As a matter of fact, other methods had been tried and had failed. In other nonrigid parts of the body the soft parts can fall together and help obliterate the suppurative focus, but this is not possible in the rigid chest. The lung is kept expanded by the negative pressure without, and coughing alone has to be relied on to expel the pus. We know that this is not always sufficient, and for this reason postural drainage has been devised and bronchoscopy has been employed to draw out pus that otherwise would be retained. If by the induction of pneumothorax one can add one more factor

course of four months. There was total collapse and the sputum disappeared. Examination two months later showed that the lung was almost entirely reexpanded. Ten months after ceasing treatment the patient was able to do full time work.

**Summary** This was a one-sided, relatively fresh postpneumonic process without severe local symptoms.

The second case was that of a man, aged 43, who had been ill for two and one-half years. He had had foul sputum for nine months. Ten insufflations were given in the course of five months, almost entire collapse of the lung resulted. Eight months later the fever had disappeared and the patient felt well.

**Summary** This was a relatively fresh one-sided moderately severe process. Almost complete collapse brought about cure without disappearance of the sputum.

The third case was that of a man, aged 39, who had had pneumonia of the lower lobe of the left lung four years previously. The sputum had gradually increased. Pneumothorax was maintained for four months and complete collapse of the lung resulted.

**Summary** This was a moderately advanced, one-sided postpneumonic process, and treatment caused little improvement.

The fourth case was that of a woman, aged 27, who eight years previously, had had pleural pneumonia in the lower lobe of the right lung, with cough, sputum and at times a rise in temperature. She had had a hemorrhage a year and a half previously. Complete pneumothorax was obtained after this process had been maintained for six months.

**Summary** This was an old one-sided process with moderately severe clinical symptoms. Because of the long duration of the illness and the fixed bronchial wall only slight improvement was obtained.

The fifth case was that of a man, aged 32, who two years before pneumothorax was begun had had pneumonia. Three months later hemorrhage occurred and the amount of sputum increased. Eight insufflations were given in the course of three and one-half months. Complete pneumothorax resulted and the sputum disappeared. Ten months later the patient felt well and did not have fever.

**Summary** The patient had a relatively fresh one-sided moderately severe process. Complete collapse of the lung after a very short time of treatment resulted in complete cure.

In a sixth case only small partial pneumothorax was obtained because of strong and diffuse adhesions. Treatment was continued and the results were negative.

In another case many unsuccessful attempts were made to obtain the pleural space could not be found. The results were negative.



The two important factors necessary for the success of this method of treatment seem to be a free bronchial outlet and a nonadherent lung. This means early cases. Another important point is that the operation should be performed under local anesthesia in order to allow the patient to expectorate during the operation, the likelihood of pus flowing over into other bronchi is thus diminished, and there is no more danger than during ordinary postural drainage.

Treatment by collapse of the lung has a practical counterpart in many of the cases of abscess of the lung which perforate spontaneously

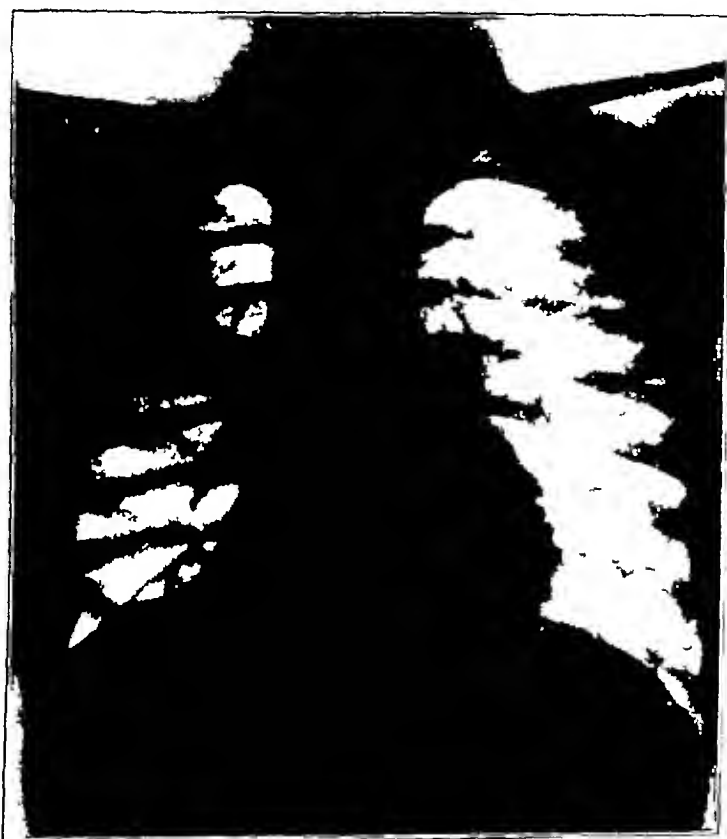


Fig. 5—Final result eight months after operation. The collapsed lower lobe seen close to mediastinum does not give rise to symptoms. Other lobes completely fill the thorax.

into the pleura and form an empyema. As is well known, simple drainage of the empyema will usually result in a cure of the underlying abscess of the lung. The curative mechanism in these cases consists of two factors: first, the drainage of the abscess; second, the resulting collapse of the affected lobe or portion of a lobe. It is even probable that actual compression of the lung may result from the combination of air and pus. After drainage of the empyema, the adhesions of the lung to the wall of the chest will help further in the obliteration by drawing the ribs inward. In this connection it may be

lung. There was much sputum and vomiting. Partial pneumothorax was obtained. Treatment was continued, the sputum decreased slightly, but increased when the treatment was interrupted.

The tenth case was that of a young girl in whom pneumothorax was maintained for three years on account of bronchiectasis of the lower lobe of the right lung. The patient became able to work full time. The foul sputum disappeared. Treatment was discontinued but after a few weeks, all the symptoms reappeared. Pneumothorax was again instituted, and the patient was well.

Goldberg and Bresenthal<sup>47</sup> reported three cases.

The first case was that of a man, aged 21, who had an abscess of the middle lobe of the right lung and who was treated for six and one-half weeks. Three injections of 1,000 cc. each were given.

The third case was that of a woman, aged 30, who had an abscess in the upper lobe of the left lung with the cavity having a fluid level. She received two injections of 700 and 400 cc. in three days.

The third case was that of a man, aged 49, who had an abscess in the upper lobe of the right lung, the cavity having a fluid level. Seven injections were given. All these patients were reported well.

Martin and Caldwell<sup>48</sup> reported a case of a woman, aged 27, who developed an abscess of the upper lobe of the right lung following the extraction of teeth. She was given a few treatments and reported cured. Details of the treatment were not given.

In 1920, Landolt<sup>49</sup> reported a case of a man, aged 22, who had had pneumonia at 5 years of age. For the last four years he had had a cough and had expectorated considerable sputum. For one and one-half years he had lost weight and had night sweats. Pneumothorax therapy was given, the duration is not known. Partial pneumothorax resulted. There was marked improvement for at least a few months.

Wessler<sup>50</sup> mentioned two cases in which artificial pneumothorax was performed, not only was there an extension of the disease, but both patients died shortly after the last insufflation. Details of treatment or of the roentgen-ray examination were not given. He concluded that the procedure was without value and might be harmful. A detailed history of the case was lacking and the cause of death was not given.

47 Goldberg B. and Bresenthal M. The Treatment of Abscesses of the Lung by Artificial Pneumothorax. A Report on Three Cases. *Ann. Surg.* 1919, 70: 169. 1919.

48 Martin C. F. and Caldwell D. M. Lung Abscess Following Extraction of the Teeth. Cured by Artificial Pneumothorax. *Ann. Surg.* 1920, 70: 451. 1920.

49 Landolt M. *Pravica-Peier* 1920, 12: 1-4.

50 Wessler Harry. Suppurative Pneumonia. *Ann. Surg.* 1918 (Dec. 27) 1919.

# RELATION OF BRONCHOPULMONARY SUPPURATION TO EMPYEMA \*

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The term bronchopulmonary suppuration is a broad one and is purposely employed to indicate suppuration within the bronchi and pulmonary parenchyma. There are three chief varieties of this general lesion: (1) the suppuration which follows the breaking down of an ordinary pneumonic process, (2) suppurative metastatic lesions during the course of a general infection, and (3) suppuration which originates within the bronchial tree (*a*) as a surface infection of the bronchial mucosa, (*b*) as retention suppuration due to obstruction by a foreign body, a tumor or a stricture or (*c*) as combinations of retention and infection. Cases of tuberculosis or actinomycosis are not included.

During the past five years, eighty-eight patients with empyema were treated in the service at Mount Sinai Hospital. Approximately 25 per cent of these cases were complicated by some form of bronchopulmonary suppuration. In practically all, the clinical course seemed to indicate that the empyema was secondary to the intrapulmonary lesion. Several of the cases occurred during a general infection, and it seems equally possible that the empyema and the pulmonary abscess were independent lesions. Most of the other cases followed pneumonia. Most of these undoubtedly belong in that large group of parapneumonic or metapneumonic empyemas which, according to the suggestion first made by Rosenbach, result from the perforation into the pleural cavity of superficial foci of liquefaction in an area of pneumonic consolidation. During the World War, the surgeons in the army were able to demonstrate cases in which the sequence was present. I have seen this condition myself a number of times on the operating table and also in postmortem specimens. Cases of this kind undoubtedly form a much larger group than one would suppose.

In clinical practice the forms of bronchopulmonary suppuration which originate within the bronchial tree are most commonly associated with obstruction by either a foreign body or a tumor. For reasons which will be described presently, I have never seen an empyema complicate this form of bronchopulmonary suppuration. Nevertheless, secondary changes occur in the structure of the bronchial tree, and bronchiectatic dilatation was found in two of the cases of this series at postmortem examination.

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\* From the Mount Sinai Hospital

with four injections of nitrogen within twelve days with marked improvement in all the symptoms. The patient recovered.

Glendening<sup>7</sup> mentioned treatment by pneumothorax of one patient with abscess of the lung but he did not state the results. In a case of bronchiectasis this treatment was used, improvement but not complete cure, resulted.

Johnston<sup>70</sup> reported the cure of a patient with an abscess of the lower lobe of the left lung following artificial pneumothorax, the abscess was due to aspiration of a piece of bone following operation on the aurium.

In 1914, Cantani and Arena<sup>17</sup> reported a case of abscess of the lower lobe of the left lung in a man, aged 35. He was treated successfully for three months; he developed a pleural effusion which was aspirated and replaced by nitrogen. The patient was free from pulmonary symptoms six months later.

Rondano<sup>6</sup> reported a case of a man with an abscess of the middle lobe of the right lung communicating with a bronchus. He was treated for three months by artificial pneumothorax, complete collapse was maintained, and eight months later the patient was in good general health and free from symptoms.

Denceau " reported two cases of pulmonary gangrene in which the patients were successfully treated with artificial pneumothorax and antigangrenous serum. The antigangrenous serum caused improvement of odor and diminution of sputum. Soon the action of the serum diminished and complete recovery took place only when pneumothorax was performed.

Denechau and others reported two other cases in which the patients were treated the same way with excellent results.

55 Glendonning L. The Use of Artificial Pneumothorax in Hemothorax, Bronchiectasis, and in Advanced Pulmonary Tuberculosis. *West J M & S* **29**: 17, 1921.

56 Johnston C H Artificial Pneumothorax in Tuberculosis  
Pulmonary Abscess and Pulmonary Hemorrhage J Michigan M S 29  
(Nov.) 1921

57 Cantani and Arena. II. Pneum storage at birth and the  
di altri affezioni dell'apparato respiratorio ed 1921 p. 81

58 Rondano I. Gangrena polmonare acuta et cilij  
Reverit de clin med 22 97 1921

59 Denochau D Deux cas de pneumothorax artificiel traités par le pneumothorax artificiel de l'école d'Anvers 25-211-1921 Denochau D Pneumothorax artificiel gangrene pulmonaire traitée par le pneumothorax artificiel associé l'un après l'autre de deux fois successives de la maladie avec succès Bulletin Société française Pneumologie 1920 45

occasions. A patient would be operated on for empyema which apparently did not have any bronchopulmonary communication. As the patient was subsequently watched, one noted that the primary pneumonia was being overcome. Then the presence of the bronchopulmonary communication would be discovered, frequently through the "gassing" of the patient during an irrigation of the empyema cavity with a surgical solution of chlorinated soda, when previous irrigations had not caused discomfort. Undoubtedly, the complete resorption of the pulmonic exudate had much to do with the "opening up" of the bronchopulmonary fistula.

In this series of cases of empyema, the pulmonary suppurations occurred in the form of soft abscesses, and they were frequently multiple. This seems to have an important relation to the subsequent formation of bronchopulmonary fistulas. In this variety there is a comparatively acute abscess formation, with soft, nondemarcating walls, it is commonly accompanied by few if any physical signs and roentgenologic evidence, and is apt to cause acute perforations between the nonadherent visceral and parietal pleurae. The outstanding histologic fact is that these abscesses do not have a surrounding area of induration. Many of these cases of empyema take the clinical form of a hyperacute pyopneumothorax; some form of bronchopulmonary fistula usually develops.

In this series, there was only one case in which an abscess existed which resembled the hard indurated form so commonly seen after a variety of other causes as, for example, after tonsillectomy. It appears that the character of the pathologic process in this form of abscess is not conducive to a comparatively sudden infection of the pleura which would produce a pleural effusion and empyema, and the large amount of indurated infiltration around the abscess cavity does not permit any sudden rupture into the pleural space. Anatomically, the lesion consists of a central cavity containing foul-smelling, brownish-red grumous pus in which a multitude of aerobic and, especially, anaerobic organisms flourish, a limiting granulation membrane of firm consistence, and a wide surrounding area of induration merging into pulmonary tissue in which fibrosis, secondary bronchiectatic dilatation and atrophy predominate. The lesion may be single or multiple, and an advanced grade of suppurative bronchitis is associated with it. An adhesive pleuritis is almost the rule and is usually limited to the area of lung involved. The process begins with obstruction of the bronchus and secondary infection. Of necessity, from the beginning a communication is present with one or more fairly large sized bronchi, more or less free drainage of the abscess into the bronchial tree is constantly present from the inception of the pathologic process.

This form of pulmonary suppuration practically never perforates into the pleural cavity. The pathologic process rarely enlarges progressively



purative process in the midst of the lung tissue. In the cases of empyema and abscess of the lung, the communication is frequently multiple, it is usually direct and extends almost always into one or more fair-sized bronchi of the second or third order, the usually profuse and foul sputum, present before operation, resembles in all particulars the pus of the abscess and of the empyema, but it immediately disappears following the adequate drainage of the empyema and of the pulmonary focus and reappears directly after interference with the drainage. Healing is tedious and prolonged, and often the bronchial fistula is an almost insurmountable obstacle to the closure of the sinus of the wall of the chest until, and perhaps even after, a radical operation is performed. In the cases of metapneumonic empyema, a communication with the larger bronchi is not demonstrable. The demonstrable fistulas are short and narrow and communicate with the pulmonary parenchyma and with the smallest or terminal bronchi. The amount of infiltration around the sinus tract is at a minimum, and the tissues are soft and pliable and have a tendency to fall together, facilities for healing are most favorable in these cases. As a rule, these communications heal spontaneously and close quickly, and they rarely cause any extraordinary prolongation of the cicatrization of the wound. Characteristically, the amount and physical appearances of the sputum are independent of the contents of the empyema cavity, it does not resemble the discharges from the wound, and depends for its production on an associated bronchitis or on the liquefaction of the pneumonic exudate which antedated the empyema.

In the cases of metapneumonic empyema in this series, a marked improvement has been demonstrated in the results of treatment as compared with the results I published in 1915. The mortality rate in general hospitals, including all kinds of cases, has fallen from 28 per cent to approximately 10 per cent. In this series of eighty-eight cases of empyema, the wounds of all but three of the patients who recovered healed completely after the primary operation and remained healed. With few exceptions the postoperative convalescence was uneventful. The great care which was taken in dressing the operative wounds and in the general treatment of the patient was thought to be responsible for the good results. All of the three patients in whom secondary operations were necessary recovered, and the wounds eventually healed.

Experiences at the Mount Sinai Hospital have led us to the belief that in cases of empyema associated with some form of bronchopulmonary suppuration healing eventually takes place in a large proportion of the patients who do not succumb to the effects of the primary illness or to some complication. Naturally, the mortality of these two factors is large. Healing will occur even when a bronchopulmonary fistula is present, if there are no other factors to interfere with the healing. Failure to heal depends on two all powerful causes (1) the

Tillman<sup>73</sup> reported a number of cases. The first was that of a young man with a unilateral moderately severe bronchiectasis who was treated for more than six years with artificial pneumothorax. His slightly purulent secretion never disappeared entirely. How clearly the process was completely healed was shown by the quick recovery from the rather severe infection at the time the treatment was being stopped. The treatment did not have any detrimental effects on the heart and did not prohibit the later reexpansion of the lung. It must be mentioned that the fact that the patient recognized his own condition made possible the long protracted treatment.

The second case was that of a man, aged 24, who had pneumonia on the right side during the influenza epidemic in 1918. He was ill for five months, several of which were spent in bed. There had been sputum and slight dyspnea since September, 1921. Marked hemorrhage occurred in February, 1922, after fever and increased cough. In March, 1922, there was no definite dullness. By Aug. 3, 1922, the patient had had nine insufflations, and treatment was still being given. A quick, good, but not complete collapse of the lung was obtained. The sputum ceased, and after eight months the condition of the patient was good. He was able to attend to work.

**Summary.** This was a one-sided anatomically moderately severe, subjectively light, case despite a duration of at least three years. The lung collapsed easily, but not completely; the sputum disappeared and the patient was reported well.

The third case was that of a man, aged 20, who had had pneumonia at 8 years of age. He had been in bed ten weeks. In 1918 he expectorated a teaspoonful of blood while coughing. For the next four or five winters, he had had long periods of coughing, but expectorated little sputum. In April 1922, the condition recurred, accompanied by high fever and considerable purulent sputum for several weeks. In August 1922 a marked hemorrhage occurred followed by several smaller hemorrhages later. In May 1923 the general condition of the patient was good. An attempt to apply pneumothorax was made, but it revealed a definitely thickened pleura. There was no air over the upper lobe, but a definite gas shadow could be seen over the lower lobe.

**Summary.** This was an old, double, anatomically moderate pneumonia. Pneumothorax was prevented by strong fibrous adhesions to the pronounced lobe.

The fourth case was that of a young man, aged 19, who was ill in March 1917. In August 1918 he had a severe influenza with several small hemorrhages. He was in bed for several months.

<sup>73</sup> Tillman: *Intern. Med.*, 1923, 1, 105.  
*Prothrombin Activity of Serum*, p. 59, 1923.



Both of these factors seem of equal importance, and the interaction of the two are sometimes sufficient to produce a vicious circle. The control of the infection is the first object, for this purpose, time is a great aid. Some of the fistulas which at first look impossible will eventually close when the infection is spontaneously controlled. The stubborn cases are due to forms of suppurative bronchitis in which an interstitial form of inflammation has occurred together with destruction of the superficial mucosa and with secondary bronchiectasis. In a few of the cases, injections of bismuth have seemed to me to be of some aid. In the most stubborn cases, it becomes necessary to destroy that part of the lung in which the sinus tract exists and in which the bronchi are the seat of this suppurative inflammation. The best way to do this is to destroy these areas progressively with the cautery at repeated sittings. Unless this infection can be controlled, practically nothing can be done toward securing a closure of the empyema cavity.

On a previous occasion, I discussed the various forms of empyema cavity which can exist with a bronchopulmonary fistula. It was pointed out at that time that unless the empyema cavity can be obliterated, the lung remains tied down and no expansion of its substance takes place, without this expansion a fistula of any size will not close. When the bronchopulmonary fistula is present with any except the smallest of empyema cavities, determined efforts must be made to secure the necessary obliteration, otherwise closure of the fistula and healing of the empyema will not occur. Time and meticulous surgical care of the wound produce astounding results. In the cases of large fistulas and large empyema cavities, it is necessary to liberate the lung mechanically (1) by freeing it at the periphery of the empyema cavity, (2) by cross hatching the granulation membrane covering the lung or (3) by both of these methods. If the lung can be brought up to the wall of the chest by these means, much is accomplished, if not, it becomes necessary to collapse the wall in order to approximate it to the lung and so secure obliteration of the cavity. I have found that the necessity for these radical measures has decreased progressively.

The final healing of any resultant fistula depends on the possibility of securing a comparatively uninfected condition of the sinus tract and the communicating portion of the pulmonary parenchyma with its contained bronchi. Unless this can be secured, the sinus tract will remain open indefinitely. The greatest obstacle to this is any bronchiectatic condition. Luckily, given sufficient time—and this seems to be an all important factor with these conditions of the chest—the sinus will gradually close.

There have been two experiences in this series in which these difficulties were encountered



There were twelve cases in this series in which the bronchopulmonary suppuration had progressed so far in the healing stage as to leave only a fistulous tract. Ten of these patients recovered. The conditions in these cases were as follows: empyema originating from a pneumonic process, four cases; recurrent empyemas with fistula, two cases; infection of the upper respiratory tract including otitis media (grippe infection), two cases; and general infection (series), two cases. Two of the patients died: one as a result of a spreading retropharyngeal abscess to which the empyema was probably secondary; the other, from mediastinitis and pericarditis.

sputum. The fingers were clubbed. Treatment by pneumothorax was given for eleven weeks, 5200 cc. of gas being injected. During treatment a slight effusion developed. The patient recovered.

The fourth case was that of a patient who had an abscess in the upper lobe of the right lung following tonsillectomy. A large amount of foul sputum was expectorated. The patient had chills and fever and lost weight. Pneumothorax failed on account of an adherent pleura. The patient did not improve.

The fifth case was that of a patient who had a chronic abscess of the left lung adjacent to the heart of eleven years' duration following pneumonia. A large amount of foul sputum was expectorated. The fingers were clubbed. There were frequent acute exacerbations. Artificial pneumothorax was caused, the patient receiving a total of 3400 cc. of gas with marked improvement. He is still under treatment.

In 1927 Jacobus<sup>85</sup> reported three cases of acute pulmonary abscess in which the patients were successfully treated by pneumothorax communicating with a bronchus.

The first case was that of a man aged 44 who had an abscess of the upper lobe of the right lung of six weeks' duration due to the aspiration of food during a vomiting spell. The sputum was purulent, fever and night sweats developed. The patient was treated expectantly for two weeks, but as he was beginning to raise more foul sputum, pneumothorax was induced and kept up for five weeks. Complete recovery was accomplished.

The second case was that of a man, aged 37, who following an acute respiratory infection had an abscess of eight weeks' duration in the upper lobe of the left lung communicating with a bronchus. The sputum separated into three layers. There were no elastic fibers. Tubercle bacilli were not found. Expectant treatment was given for two weeks, then pneumothorax was induced and maintained for nine months. The patient recovered.

The third case was that of a man, aged 47, who, following acute respiratory infection had an abscess of the upper lobe of the right lung communicating with a bronchus of four weeks' duration. He raised a cupful of foul purulent, coffee-colored sputum which separated into three layers and contained bacteria of different kinds. Tuberculosis did not occur. Pneumothorax was induced and maintained for four months. He made a complete recovery.

Pettingill<sup>86</sup> reported the following case. A man aged 38, while working in the mill in Haverhill in February, 1919, developed a severe

<sup>85</sup> Jacobus, H. C. Some Cases of Acute Pulmonary Abscess Treated by Pneumothorax, *Acta med. Scandinav.* 65:697, 1927.

<sup>86</sup> Personal communication to Dr. Gerardo M. Balboni by Dr. Olin S. Pettingill of Essex County Sanatorium, Middletown, Mass.

tion incidental to the pneumothorax which results. Death occurs, not from the disease per se, but from untimely and careless interference by the medical or surgical attendant.

The febrile state of the patient, the elevation of temperature, rapidity of the pulse and respiratory rate, the degree of dyspnea and the toxic condition of the patient generally indicate treatment by aspiration first, and by some type of drainage subsequently.

It is difficult to lay down hard and fast rules for the treatment in so variable a type of disease as acute empyema. The routine procedure employed by me for the past ten years has been as follows, the operator being guided by the patient's condition.

1 Aspiration is performed in the early stage of the disease. If the fluid is thick, air replacement may be employed to hasten the flow of the fluid through the needle.

2 When the patient is not improving, closed drainage is established by the catheter and cannula method, inserted through a dependent interspace and led off to a Winchester half full of water, which is suspended under the bed.

If the fluid is thick, a second catheter may be inserted in the highest space adjacent to the cavity, and the cavity will be irrigated through the upper catheter while it empties through the lower one.

As the tract about the catheter enlarges, a larger tube is inserted, and if the temperature is maintained and the cavity is not reducing appreciably, two or three small Carrel tubes are inserted through the opening and carried on pliable lead sounds to the upper portions of the cavity and irrigation with surgical solution of chlorinated soda is (Dakin's solution) begun.

Forced blowing exercises every hour by the use of large Wolfe bottles are encouraged.

3 If the patient is still not doing as well as is expected the tract of the catheter opening is excised, the incision is extended either way and the thorax is widely opened in the interspace. The cavity is explored with a lighted retractor (Adson's brain retractor), adhesions severed, fibrinous deposits cleared out manually and all encysted or nondependent cavities rendered dependent. Carrel tubes on lead carriers are inserted and irrigation with a surgical solution of chlorinated soda is carried out, every two and a half hours.

4 Should there be any difficulty in gaining and maintaining easy access to the cavity through an interspace, we do not hesitate to resect a rib, widely, being careful to have our opening at the lowest portion of the cavity. Occasionally, after first opening the chest in the interspace and finding that the incision is not dependent, it is necessary to insert the hand and make an opening in a lower space directly on the fingers inserted through the chest. In such an instance, the upper incision is usually closed completely, and the lower opening is maintained.

During the acute stage, patients are placed on forced feeding with highly nourishing foods. Alkalis and dextrose are given by mouth, and small transfusions of blood of from 300 to 500 cc are given and repeated as often as necessary if the patient does not rapidly overcome the toxemia.

Local anesthesia or modified paravertebral anesthesia, if necessary, associated with gas and oxygen analgesia, or better, ethylene analgesia is employed for all operative measures during the acute stage of the disease.

ACUTE PULMONARY SUPPURATION  
SELECTIVE ACTION OF ARTIFICIAL PNEUMOTHORAX  
IN THE TREATMENT OF THIS DISEASE

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AND  
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Of the various methods of treatment advocated in cases of acute nontuberculous intrapulmonary suppuration the induction of artificial pneumothorax has received scant attention. Many writers do not mention it and others vary from unqualified recommendation to condemnation of the method.

Kuttner<sup>1</sup> for instance emphatically condemns Jorlann's method of artificial pneumothorax in the treatment of abscess of the lung by saying that he believes the spontaneous cure is favored by coughing and expectorating and that pneumothorax prevents this and favors the stagnation of pus. As a result there is great danger of pus flowing over into other bronchi leading to the formation of fresh foci of bronchopneumonia and multiple abscesses.

In 1924 Lambert and Miller,<sup>2</sup> in an analysis of sixty cases of abscess of the lung stated that their experience with the method of artificial pneumothorax had been limited as they had used it on only seven patients none of whom improved and two of whom died. In a more recent analysis of 100 cases by the same authors the following opinions are expressed:

We have employed this method in some cases but tentatively, in order to have gained experience as a basis of judgment rather than with great confidence in it as a rational procedure. The reason for this somewhat experimental method of approach is found in our conception of the radically different objects to be attained in pulmonary tuberculosis as opposed to abscess of the lung. In tuberculosis rest and immobilization of the lung appears to us to be the prime consideration and for this often partial pneumothorax without any actual compression of the lung is adequate.

In abscess drainage is the desired object, and by artificial pneumothorax this can only be facilitated by pressure properly applied upon the right point and in the right direction. We do not feel that this can be accurately gauged in artificial pneumothorax. Moreover it sometimes happens that the air introduced works around into the pleural space near the mediastinum and may actually cut

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1 Kuttner in Bier, Braun and Kummel. Chirurgische Operationslehrer, Leipzig, J. A. Barth 1923.

2 Lambert and Miller. Abscess of Lung Arch Surg 8:446 (Jan) 1924.  
Lambert. New York State J. Med 27:47 1927.

closure by muscle or skin flap, limited resection of the wall or some allied simple method is preferred because of the saving in time to the patient.

In patients with larger cavities, there is a diminution in the air-bearing capacity of the lungs, and every effort should be made to reexpand the collapsed lung, with a view to restoring the normal vital capacity.

While the apt surgical dictum "*ubi pus, evacua*" does not always apply to patients with acute empyema, it does apply to those in the chronic stage of the disease. Before any extensive operative intervention is undertaken, the cavity should be thoroughly irrigated with surgical solution of chlorinated soda until the lung no longer expands and the discharge is as nearly sterile as possible. Then decortication is planned, if necessary, associated with a partial resection of the bony wall of the chest and thickened parietal pleurae covering the cavity. Lloyd,<sup>9</sup> I believe, was the first to undertake decortication in this country. Fowler<sup>10</sup> described his method of decortication in 1893. Decortication of the visceral pleura properly performed, when followed by complete expansion of the lung, is one of the most satisfactory operations in modern surgery. Unfortunately, in inexperienced hands, or in the hands of the surgeon who only occasionally undertakes such a procedure, the operation is difficult, it is fraught with dangerous possibilities and sequelae recognized only by those who have carried out the operation many times and who have had the intimate after-care of such patients. In addition, it has been our experience that one cannot foretell how completely the lung will expand following decortication. The duration of chronic empyema seems to bear little relation to the ability of the lung to expand. We believe that the degree of expansion depends on the nature of the inflammatory process that originally existed in the lung tissue adjacent to the cavity. For some years, we have as a policy excised a small nodule of the lung when expansion at operation has been limited, and in every instance we have found that various degrees of fibrosis exist which prevent expansion of the lung tissue itself. Care must be taken when this section is made. The cautery is applied to the surface to sterilize it as in autopsy work—the small section is excised with a knife and oversewed, and a small pedicle of fascia is tied over the area of suture. Fowler's patient, a woman, aged 35, had had the cavity for ten years. Expansion was complete in this case. We have obtained complete expansion in a patient whose cavity had existed sixteen years, and two-thirds expansion in a cavity of twenty-one years' standing, but we have repeatedly had less than 50 per cent of expansion in cavities that have been present less than one year. I am personally convinced that the tissue of the lung undergoes a repair process as time goes on, with

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9 Lloyd. Personal communication.

10 Fowler, G. R. M. Rec., Dec. 30, 1893, p. 838.





tions within the thorax, and to allow the wall to collapse partially at least to meet the expanding lung

Such procedures as the modified operations of Estlander and Schede are still necessary. The operation of Wilms, i. e., resection of a one-half inch segment of several ribs at their angles posteriorly, and at the costochondral juncture anteriorly, while not commonly employed, is of value in those patients in whom one lung is practically totally collapsed. In all osteoplastic operations, the procedure must be planned so as to allow sufficient shrinkage of what might be described as the roof of the cavity, so that every portion of it comes in direct contact with visceral surface of the underlying and expanding lung. Care should be taken to remove one rib too many rather than one too few. For that purpose, we remove the rib above and below the cavity throughout the length or width of it, according to the position. In most instances we excise the thickened parietal pleura intact with the ribs, so that finally muscle tissue comes in contact with visceral pleura. In removing the roof of the cavity, the skin and muscle flap is turned back intact down to the ribs, the ribs themselves are not stripped of their periosteum, except to allow sufficient space to sever them with the bone forceps, and the upper and lower incisions through the roof pass through the intercostal muscles rather than through the stripped periosteum of the ribs. Parietal decortication itself cannot be too strongly condemned because of grave primary and secondary hemorrhage from intercostal vessels.

Operations designed by Korte, Hellstrom and others of the European school to remove portions of the scapula should not be encouraged. There are a small percentage of patients, however, in whom some of the lower half of the scapula must be removed. This should be done subperiosteally, and there must be no interference with the muscles and nerves. Pediculated muscle and skin flap operations are extremely valuable and must be adapted in some form to most cases. The divided U-shaped flap as suggested by Robinson is most valuable in peculiarly shaped and placed cavities. In a small percentage of cavities placed high anteriorly and directly in the upper portion of the axilla, we have been obliged to unroof the cavity entirely and to expose it completely, in all but one patient we have managed to cover the exposed pleura with skin at once or gradually, either by encouraging the skin edges to granulate in by the use of balsam of Peru or Ochsner's method of using adhesive tape or by skin graft.

We have had little success with the use of bismuth paste, and we rarely employ it. I have so much respect for the work of Emile Beck<sup>15</sup> that I would not condemn its use, but credit our failure to cure even small cavities with it to improper or injudicious use of it.

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15 Beck, E. M. Toxic Effects From Bismuth Subnitrate, J. A. M. A.  
52:14 (Jan. 2) 1909



presented by Dr Santee<sup>16</sup> at a meeting of the New York Surgical Society in which undoubted massive collapse of the lungs without bronchial obstruction was found at autopsy

Dr Eggers speaks of his case as illustrating the selective action of pneumothorax. The actual mechanics of the so-called selective action of pneumothorax is splendidly and convincingly illustrated in an article by Bendove<sup>17</sup>. Anybody who can study his pictures and not be absolutely convinced concerning the way that mechanism acts must be hard to convince.

Dr Eggers said that there is less circulation in a collapsed lung than in an expanded lung. I believe that is not the result obtained by the physiologists. In a collapsed lung, such as results when there is air in the chest but the lung is not compressed, when there is no positive pressure of the pneumatic type but the pressure is normal, it has been stated (Yates<sup>18</sup>) that there is an increase instead of a decrease in the circulation in the vessels in the lung.

I think Dr Yates has made use of this principle as a part of his ingenious method in the treatment of patients with tuberculosis by crushing the phrenic nerve to produce temporary paralysis.

Dr Pickhardt's paper greatly interested me and it showed how observations made at roentgen-ray examination and clinical signs are not always similar.

He demonstrated a normal chest in which first-class diagnosticians had stated that pneumonia was present. I will not try to make an explanation. I only say that it is necessary to have the clinical picture of the case and then to match up the conditions shown by the roentgen-ray examination the best way possible. One may not be able to read the roentgenograms correctly, but the appearances cannot be contradicted.

The case of Anna Rosta was one that I shall not forget. The picture looked like a massive collapse, in fact I believe that the condition was a massive collapse. The heart had been pulled entirely into the affected side.

The traumatism probably had something to do with the abscess. I think Dr Pickhardt has done a good thing in showing us what I have always believed, that so-called unresolved pneumonia is more apt to require surgical treatment than medical.

DR HUGH AUCHINCLOSS, New York. Dr Pickhardt brought out what has become more and more evident to all of us, namely, that unresolved pneumonia is a rarity, and that most cases in which that diagnosis is made are sooner or later shown to be cases of a different condition.

As regards the paths of extension of infection to the lungs and pleura, it is extremely interesting to hear of the enormous number of tonsillectomies that have been performed without the formation of an abscess of the lung.

It seems unwise to confine the path of extension by any one route. It seems to me to be unwise to assume that aspiration is always responsible for extension or that emboli are always responsible. Another route, which seems perhaps to be most important, namely, that route along which the lymphatic stream flows, really is the architectural scaffolding of the lungs, and of course, the blood and lymph vessels are in this same scaffolding. The extension of

16 Santee. *Ann Surg* 85 608 (April) 1927.

17 Bendove. The Mechanism of Localization of Gas in the Pleural Cavity and Its Clinical Application in Pneumothorax Therapy, *Arch Surg* 13 369 (Sept) 1926.

18 Cloetta, quoted by Yates. *Surgery in Pulmonary Tuberculosis*, *Arch Surg* 14 372 (Jan) 1927.



Embolism is the cause of abscess of the lung in many cases, but the majority of cases of abscess of the lung are due to aspiration. At least I and many others believe that this is true.

It was instructive to hear Dr. Crowe speak of the experiments that had produced abscess of the lung in dogs by aspiration after the pus had been heated. I understood him to say that microbes act differently when suspended in a cool fluid.

It was, furthermore, extremely illuminating to hear Dr. Crowe say that they succeeded in introducing cotton containing microbes from pyorrhea cavities into the frontal sinus of the dog and were thus able to produce abscess of the lung in the majority of cases by gradual aspiration of the secretion from the infected sinus.

Regarding diagnosis, our country is advancing ahead of the majority of other countries in that bronchoscopy is used early in these cases.

In our well conducted hospitals there is prompt cooperation between the various departments. The diagnosis is not simply left to the internist and the surgeon, everywhere the roentgenologist and bronchoscopist are called in at once. We work hand in hand—physician, surgeon, bacteriologist and roentgenologist, and then we promptly call on our experienced bronchoscopist.

And so it has come about that we follow a certain course of events in making the diagnosis in establishing the indication for treatment and in starting treatment. As Dr. Kernan said this morning, let the bronchoscopist take the case in hand first, if it is not a case for prompt surgical intervention.

Personal observation has impressed a few points deeply on my mind. It was hard for surgeons at first to transfer these cases to the bronchoscopist, but the results that I saw were so phenomenal that I considered it the duty, not only of myself but of every general or thoracic surgeon called on to perform these operations, to refer the patients first to a trained bronchoscopist.

Dr. Kernan reported a case of the late Dr. Lynch who was consulting bronchoscopist at our hospital for a number of years. The woman, one of my patients, had foul expectoration which developed following aspiration after tonsillectomy. She had high fever, but fortunately came in a few days after the condition developed. Dr. Lynch made one of his splendid inspections and performed aspiration. All the threatening symptoms quickly disappeared, not only the rise of temperature and the general malaise, but the expectoration. It was hard to believe that a single seance of bronchoscopy and aspiration could accomplish such a result. The patient left, and it was hard to trace her again. We ascertained that she was well after three or four years.

Then, in preparing a paper on suppuration of the lung and collecting and following-up cases of patients whom we had treated, we were astonished to find that not only patients with an acute condition were cured by bronchoscopy, but also that those with subacute and even chronic cases were much improved, some were cured.

That peroral endoscopy cannot cure them all is understood but, to my mind, it is the duty of every surgeon to call on the experienced bronchoscopist first and let him show what he can do, not only by aspiration, but by conscientious and faithful endobronchial treatment. If he fails, the case will become one for surgical measures.

We know that spontaneous healing without surgical intervention occurs in about one third of the acute cases due to aspiration, of course, I shall consider these principally because I believe that aspiration is the most frequent etiologic factor. We should make it clear to ourselves that it is impossible to find out

pointed out that such perforations usually occur only in the early stages of an abscess near the surface with thin walls, and not in chronic abscesses with thick, rigid walls and a surrounding area of fibrosis. It also seems apparent that in only comparatively recent cases of abscess is artificial pneumothorax suitable for treatment, i. e., in cases in which the lung is compressible and in which there is a good outlet to the main bronchus.

These various considerations make us feel that there is a rational basis for treatment by artificial pneumothorax in cases of acute suppurative intrapulmonary lesions, and that in properly selected cases it may prove to be of great value.

DR CARL HEDBLÖM, Chicago Nontuberculous pulmonary suppuration is a comprehensive subject to cover in a short symposium, and obviously only a few points can be touched on in a few minutes' discussion

The papers presented bring out facts which seem to me to be of fundamental importance to our understanding of the subject. The question of the etiology of abscess of the lung interests me, not so much as an academic discussion, as because of its practical importance. Precautions against aspiration of infected material, particularly during operations on the nose and throat, could be largely abandoned if we were to accept without further question the results of experiments on animals purporting to show that pulmonary abscess following such operations is, as a rule, a blood-borne infection.

The experiments on animals cited in support of this view seem to me do not warrant such an assumption. We know that if gross infected material is introduced into the general venous circulation, it will be sifted out in the lung, and that abscess of the lung should follow does not seem surprising. But this does not prove that this is the mechanism by means of which infection reaches the lung in man following tonsillectomy, for example, nor does it exclude the possibility of infection by inhalation. Furthermore, the failure to obtain abscess of the lung in the dog in a hundred animals or less loses significance when it is considered that the incidence of abscess in man is only one in several thousand.

It has also been shown that pulmonary abscess may be produced in dogs and other animals by infection by inhalation. Other considerations also point to infection by inhalation as playing the most important rôle in postoperative pulmonary abscess. Among such may be mentioned the ease with which animals inspire foreign material into a bronchus during anesthesia, the demonstration of blood in the trachea in a large proportion of patients following tonsillectomy, the relatively large proportionate incidence of postoperative abscess following deep general anesthesia, particularly if the patient is operated on in the sitting position, and the finding of teeth or fragments of them following extraction under general anesthesia in abscesses producing similar clinical manifestations. Such abscesses that I have opened have been situated in the periphery of the lung. Furthermore, precautions against aspiration of infected material, local anesthesia or light general anesthesia, with the head lower than the body, suction, careful hemostasis, etc., have reduced the incidence of post-tonsillectomy abscess to almost nil in many clinics with a record of thousands of cases each.

Dr Crowe's experimental production of pulmonary abscess in dogs following infection of the frontal sinus seems to me to be of fundamental importance. The resulting discharge of pus into the nasal passages would seem to furnish conditions favorable for inhalation, but not for blood-borne infection in the lung.

The treatment for pulmonary suppuration, as Dr Lilienthal has properly emphasized, must be individualized. The term includes essentially abscess, bronchiectasis and their combinations. Pulmonary abscess may be single, multilocular or multiple, central or peripheral, acute or chronic, and treatment to be rational must necessarily take into account the varying pathologic processes and location. The various methods of treatment—postural drainage, bronchoscopic dilatation and lavage, pneumothorax collapse and thoracotomy drainage—find their indications according to the nature and location of the abscess.

A centrally located abscess—near the hilum—is the type most suited for conservative methods: postural drainage, lavage, pneumothorax collapse. Such

Bronchiectatic dilatation, with the exception of certain congenital and generalized forms, is constantly met with in suppurative foci within the parenchyma of the lung. This seems to be related to a destruction of the elastic fibers which normally form such an intimate and important structural item of the bronchial wall. In sections of lung tissue in which suppurative processes are taking place, this destruction forms a prominent part of the histologic picture.

Suppurative metastatic empyema usually indicates an embolic lesion either in a small vessel of the pleura or in superficial parts of the lung. In either case, a focus of suppuration forms which ruptures into the pleura. In cases of general infection, foci of infection of this variety are frequently found in the midst of the parenchyma of the lung as so-called "furuncles", only those result in empyema which are sufficiently near the visceral pleura so that it is mechanically easier for the pus to rupture into the pleura than into the bronchial tree.

In approximately 71 per cent of the cases of bronchopulmonary suppuration and empyema in this series of cases of empyema, some form of bronchopulmonary fistula existed which communicated with the operative wound in the wall of the chest by way of the empyema cavity. It is likely that more of these existed, but in the other cases the fistula was undemonstrable. A distinction should be made between those fistulas which reach into any but the smallest of the bronchi and those which reach into the pulmonary parenchyma. The first of these are easily recognized, are fairly large, are sometimes multiple, are associated frequently with large empyema cavities and with collapsed lungs, are difficult to heal, commonly are subject to secondary operations and frequently persist in spite of all that one can do. The second are difficult to recognize, except by the test with a surgical solution of chlorinated soda (Dakin's solution). They are associated with smaller empyema cavities, usually do not materially delay the healing of the cavity and practically never are a sufficient cause for secondary operations, in almost all of the cases, the empyema cavity heals.

In metapneumonic empyema, the disturbance created by the production of the empyema is commonly at a minimum. The nature of the process lends every assistance to this condition. Commonly there is a preexisting pleurisy over the involved area, and adhesions usually occur. The progression of the lesion is comparatively slow, the rupture of the superficial abscess takes place concomitantly with its efficient localization by adhesions, and the static conditions within the thorax are not disturbed. The communication with the interior of the pulmonary parenchyma is comparatively small and is further rendered futile, often only temporarily, however—by the pneumonic exudate surrounding and plugging it, thus effectually blocking any immediate free communication with a bronchus. I have appreciated the latter fact forcibly on many



ported by the cellular and noncellular elements delivered in the blood. Adequate repair leads to undelayed healing which in structures of the lung can be well nigh scarless. Inadequate repair protracts convalescence, increases cicatrization, and inflicts permanent disabilities of a peculiarly burdensome type, because they impair cardiac as well as pulmonary functions.

Bronchopulmonary structures possess extraordinary native powers of resistance, defense and repair which differ little between individuals. Susceptibility to infection, inadequate defense against infection and inadequate repair of tissue destroyed by infection are attributable mainly to deficits in the quality of blood delivered to the affected lung.

The obvious obligations of therapists in combating pleurobronchopulmonary inflammation are (1) to help improve the quality of blood in circulation, (2) to promote deliveries of the maximum unit volume of blood to unit volume of affected lung, (3) to reduce but not to abolish the excursions of the lung because abolition would cause hypemia, and (4) to minimize cardiac effort.

1. Quality of blood in circulation improves with rest, diet, fresh air, sunshine, medication by mouth or intravenously, and transfusions of unmodified blood repeated as needed. Blood transfusions are supposed to be dangerous or useless in treating persons with intrapulmonary conditions, and, as frequently given, this is correct. Too large transfusions of blood and those given too rapidly cause acute cardiac dilatation which often kills. Blood treated with the anticoagulants now available is unduly irritating, it frequently provokes severe, and occasionally some lethal, reactions. Its leukocytes are injured, and, more significant still, the antibody content, the most serviceable of noncellular elements, is impaired.

2. Maximum unit volumes of blood are delivered to unit volumes of lung when the lung is in a position of incomplete deflation corresponding to reduction but not to abolition of intrapleural negative pressures. In this position, the intrapulmonary vessels are neither more tortuous as in more advanced deflation nor more elongated as in greater inflation. Peripheral intravascular resistance is least, and cardiac power propels the most blood.

3. Reduction but not abolition of pulmonary excursions occurs when the excursions of the thoracic parietes are correspondingly restricted.

4. Cardiac effort is least when the peripheral intravascular resistance is least. This obtains if the excursions of the lung are restricted to those just above and just below the mean between full inflation and full deflation, and the patient is inactive.

A lung can be placed in the most propitious position which at once raises its powers of resistance, defense and repair to the optimum and minimizes cardiac labor by two procedures. Pneumothorax can be induced if pleural adhesions are absent, and the intrapulmonary negative pressures reduced. This adds another irritant, provokes pleuritis, is transient and cooperates but inexactly with natural responses. The diaphragm may be paralyzed by the blocking of the branches of the phrenic nerve that transmit motor impulses to the diaphragm. This exactly resembles the responses in man and animals to divers forms of spontaneous and induced pleuropulmonary irritations. Paralysis of the diaphragm automatically restricts costal excursions and assures the physical conditions most favorable for recovery. Paralysis and consequent elevation of the diaphragm, partial pulmonary deflation and reduced vital capacity are undesirable in health. Paralysis can be made transient by temporary blocking of the phrenic trunks bearing motor impulses (*phrenemphraxis*), or, when indicated, permanent palsy is induced by extracting those trunks (*exeresis*).

within the pulmonary parenchyma until the surface of the lung is reached and the visceral pleura is destroyed. As adhesions between visceral and parietal pleura have preceded this advancing destruction, an abscess cavity is produced, one wall consists of lung tissue and the other of the parietal pleura lining the interior of the thorax. These cavities are usually circumscribed, and they most commonly exist in the posterior angle of the lung near the ligamentum latum pulmona, they are less commonly present in the lateral aspect of the lung.

Clinically, this lesion is sometimes mistaken before operation for a localized empyema of the ordinary variety, and the pulmonary origin is surmised only when the physical characteristics of the cavity are determined on the operating table. Multiple bronchial fistulae usually occur. The pathologic picture reproduces that artificially made many times when operations are performed for bronchopulmonary suppuration without empyema, especially when a bronchostomy is established. Clinically, the course in this variety of bronchopulmonary suppuration with empyema is satisfactory after simple incision and drainage, the fistulas close spontaneously, and the wound heals in the largest proportion of the cases.

The observations made in regard to the mechanism by which lesions of the lung (pneumonia and bronchopulmonary suppuration) are complicated by empyema are most important, as they teach that the commonest varieties of this disease ordinarily occur only in the presence of a destructive lesion in the pulmonary parenchyma the progression of which secondarily involves the pleura by acute perforation or by chronic penetration. So far as the empyema is concerned, there is no essential difference in the mechanism, whether the primary lesion is pneumonia or whether it is an abscess of the lung, the important point to remember is that in either case there is necessarily present a communication with the interior of the lung or the bronchi or both. The difference, if any, is one of degree of virulence and toxicity of the offending organism, of the rapidity with which the process advances, with which the lung tissue is destroyed and with which the perforation takes place. The result varies with the presence or absence of pleuritic adhesions near the pulmonary process, with the size of the perforation and its communicability with one of the larger bronchi. The size of the latter has mathematical relationships with the character of the initial pneumothorax, with the resultant disturbances of the static and dynamic conditions within the thorax and with the severity of the clinical manifestations presented. The whole picture is built around the presence of a bronchopulmonary communication.

The demonstration of a bronchial fistula therefore necessarily furnishes indubitable evidence of the presence or preexistence of a sup-

empty into the thoracic duct or the large veins. There is no flow of lymph from the head to the lungs, and many valves protect the lungs against backward flow from bronchial and pulmonary lymph nodes. These lymph nodes have afferent and efferent vessels, and if infectious material passes the last of the nodal chain, it will be poured through the thoracic duct into the right side of the heart and directly to the lung as from the cervical lymph nodes. When bronchial and pulmonary lymph nodes are infected from the head, they have received that infection from the lung, which has been infected by aspiration or by blood from the right side of the heart. One must always remember that a lymph node may rupture, this is an exceptional occurrence, however.

When dealing with chronic lesions of the lung, tuberculosis must first be excluded. This is not easy. Roentgen-ray examination is essential, but may not be sufficient. The subject is too large for this discussion. It is, important, nevertheless, that the bronchoscope should not be passed, iodized oil injected or operation considered until the existence of tuberculosis has been proved or disproved.

The discussion of unresolved pneumonoma brings up the question of tuberculosis. The basal type of tuberculosis is a form of unresolved pneumonia, and one is not able to differentiate the various etiologic factors by roentgen-ray examination.

I know of no place in the world where one can learn more about lesions of the chest than one can at these meetings.

DR FREDERICK T. LORD, Boston. I should like to refer for a moment to unresolved pneumonoma which as an internist I feel I should defend before a body of surgeons. It has been spoken of as of rare occurrence. In our experience, organizing pneumonia is found at autopsy in about 7 per cent of the cases of genuine croupous pneumonia, and this proportion is sufficiently high to warrant its consideration as a real condition, as Dr. Pickardt suggests, in any group of complications such as those he presents. In exceptional instances, as in six of our series, organizing pneumonia was found at autopsy within from seven to seventeen days of the onset of acute pulmonary symptoms, ordinarily, however, in clinical cases a delay in resolution beyond three weeks may be regarded as evidence of developing organization and induration, provided pulmonary tuberculosis, empyema and abscess of the lung can be excluded. Improvement in roentgen-ray technic and in the interpretation of roentgenograms make it comparatively easy to avoid confusion of unresolved pneumonia with other conditions.

The explanation of unresolved pneumonia is doubtless to be found in the chemistry of the exudate. Resolution is probably accomplished by local increase of cells (enzyme), diminution of serum (anti-enzyme) and shift to an acid reaction. Delayed resolution may be ascribed to a disturbance in the local ferment-antiferment balance. If there is a shortage of cells or an excess of serum, resolution may be delayed or fail to take place.

Referring to bronchoscopy in diagnosis and treatment, bronchoscopy is chiefly of service in the recognition of bronchial occlusion which occurs with surprising frequency in connection with bronchopulmonary suppurative lesions, and which is usually due to a foreign body, tumor, granulation tissue or a cicatrix. I especially want to emphasize, without going into detail, that important evidence may be obtained regarding the presence of bronchostenosis by other means than the use of the bronchoscope. It should be appreciated that there is a significant evolution and grouping of symptoms when a foreign body or tumor is the cause of the disturbance. As regards physical signs, there may be indications of

constant reinfection of the empyema cavity from the interior of the lung by way of the bronchopulmonary fistula and (2) certain static and dynamic conditions which have to do with the relative size of the main bronchus, the opening in the wall of the chest and the size of the fistulous tract

There are two causes for reinfection of the empyema from the interior of the lung (1) an undrained or incompletely drained abscess of the lung, and (2) a persistence of infection in some part of the bronchial tree in relation with the sinus and the empyema. Both of these are equally important, and of the two, it is most difficult to contend with the persistence of infection in the bronchial wall. A pulmonary abscess is frequently prevented from healing by the smallness of the opening by which it is drained. Infection in the bronchial tree (suppurative bronchitis) is kept up (1) because of the character of the organisms which are present, (2) because of constant reinfection from a communicating abscess of the lung and (3) because of small areas of necrotic bronchial cartilage in some cases. In addition, the bronchiectatic dilatations usually alternate with lengths of bronchi in which relative strictures are present, and retention of pus occurs in the dilated parts.

Under these conditions, the pulmonary focus plays a more important rôle than the empyema proper, and in order to cure the patient of empyema, the pulmonary lesion must be brought under control. In my cases of empyema, the main problem has been more rarely that of the bronchopulmonary suppuration. It is my experience that the area of involvement of the lung gradually grows smaller, if given sufficient time and if proper drainage is kept up, until all that is left is one or more fistulous tracts.

The cases in which this spontaneous retrogression has not occurred have been comparatively few in my experience and have been associated with more or less marked grades of secondary bronchiectasis. In the latter, one can either perform a lobectomy when conditions are ideal or one can increase the facilities for drainage. Lobectomy is extremely dangerous under the conditions. Bronchostomy, however, is a much safer procedure, and when properly performed so that complete drainage is established, the induration surrounding the abscess gradually disappears. Partial lobectomy performed with the cautery is only a form of bronchostomy.

The resultant bronchopulmonary fistula has been the more frequent problem. Those that give the most trouble are associated with bronchopulmonary forms of suppuration. The plan that I have found to be the best has comprised two objects (1) the control of infection within the sinus and the bronchial tree so that one could have comparatively uninfected territory to deal with and (2) the obliteration of the empyema cavity.

lung, or empyema which has ruptured back in the lung. All of the cases occurred in adults, and all were characterized by a history of the patient's having had, about a year previously, an acute inflammatory disease of the lung that had quieted down and had left the patient only moderately ill and without fever, but with a daily output of sputum, little appetite, and unable to continue his work. Regardless of the exact character of the lesion, as it had been present for a long time and was situated in the lower lobe, it seemed reasonable to assume the fixation of this lobe by adhesions and further that, with the lower lobe so fixed, the rise of a paralyzed half of the diaphragm would result in definite though perhaps incomplete collapse of this diseased lobe. We tried blocking the phrenic nerve, and in a number of instances achieved the

DR E. F. BUTLER, Sayre, Pa. Simple drainage operations for pulmonary suppuration have yielded disappointing results. A lack of adequate operative access to the suppurating area and a lack of adequate postoperative control have constituted obstacles to the attainment of satisfactory end-results. Recently more satisfaction has been obtained from radical operative programs. A series of fourteen cases have provided 75 per cent of complete cure and a return of the patients to economic life. An additional 5 per cent promise to reach this same goal. In 12 per cent, the object has not been accomplished. The mortality has been 8 per cent.

The basic strategy in these cases has been to conserve lung tissue and function at the expense of the anatomic structures of the chest wall proper. The tactical accomplishment has depended on creating a wide window in the wall of the chest overlying the pulmonary lesion, and through this to maintain tactile and visual control over the suppurating area until it has become clean enough to permit of closure of the defect in the wall of the chest by a skin-muscle flap prepared at the first stage operative approach.

DR FRANK TORFK, New York. I should like to make a remark in reference to the academic question which has been brought up as to whether there is more blood or less blood in the lung after collapse. All matter is subject to certain physical laws, and the lung is no exception. If pressure is exerted on any part of the body, for instance on the skin, there will be less blood in it, it will be blanched. If, on the other hand, suction is applied, the pressure thereby being diminished, the result will be more blood under the area so treated. If neither pressure nor suction is used, and the condition normal, the amount of blood in the part will be intermediate between the two extremes of diminution by pressure and increase by suction. In the case of the lung, there must be, as Dr. Lilienthal said, a diminished amount of blood, if the lung is compressed. I do not think anybody will deny that. But there seem to be differing beliefs as to the relative amount of blood in the collapsed (not compressed) lung and the distended (normal) lung. If a collapsed lung is brought into a negative pressure chamber, so that it will expand to the normal dimension, there is an exact counterpart of the skin area mentioned before as being under the influence of suction. By thus diminishing the pressure on the outer surface of the lung, a greater amount of blood must infallibly be drawn into the organ. In the normal thorax this condition of diminished pressure, negative pressure, on the outside of the lung constantly exists, nature establishing it so that a maximum amount of blood may be sent to the lungs for oxygenation, and with each inspiration the suction on the outer surface is increased with a consequent increase in the amount of blood entering the lungs, whereas the expiratory effort drives it out again. The parallel between the blood in the lung and that in the area of skin mentioned before may seem

## REPORT OF CASES

CASE 1—A young woman developed a posttuberculosis abscess of the lung and a pyopneumothorax. The empyema was drained and a bronchostomy was established. Multiple bronchial fistulas were present and a copious discharge of mucus persisted for months. Then the indurated portion of the lung was progressively destroyed with the cautery, and subsequent roentgenograms showed a progressive diminution of the indurated area. Clinically, there was a similar diminution in the amount of the discharge and a coincident marked improvement in the general condition of the patient. At the present time, there is a comparatively small shallow cavity lined with granulation tissue, in the bottom of which are a number of minute bronchopulmonary fistulas. The discharge is at a minimum. Time will be a great aid to this patient.

CASE 2—Following incision for a large empyema with collapse of the lung a young man had a large cavity in which bronchial fistulas were present. A roentgenogram of the chest showed an absence of an indurative process in the lung. Finally a thoracoplasty was performed in which the wall of the chest was collapsed. The wound healed down to several narrow sinuses, which persisted for more than a year before they closed. When this article was written one year ago the wound had remained completely healed.

Epithelialization of the sinus tract so that a bronchopulmonary cutaneous fistula results is a theoretical obstruction to the final healing of any fistulous tract, I have never seen this in bronchopulmonary fistulas, either clinically or in the laboratory. While I am ready to admit that the condition is possible in large-sized fistulas which reach directly to the skin, I am convinced that if all other impediments to the healing of the sinus are removed, epithelialization of the sinus becomes an inconsequential factor.

There were six cases in this series of bronchopulmonary suppuration with empyema in which a bronchopulmonary fistula was not demonstrable at any time. Four of these patients died: one from multiple abscesses of the lung, another from a suppurative pericarditis after pericardiostomy, a third, from a pulmonary embolism, and the fourth from the effects of a general infection. The last mentioned patient also had multiple abscesses of the lung.

The absence of any bronchopulmonary communication with the empyema cavity seems to increase the gravity of the pulmonary lesion; the number of fatalities are correspondingly large, and are due to the condition of the lung. As soon as this communication becomes established there seems to be an amelioration of the entire condition. This seems to agree with the results obtained in cases of bronchopulmonary suppuration without empyema after a bronchostomy has been performed. The improvement which follows is directly proportionate to the extent and freedom of the drainage which is established.

Tufter called attention to the fact that 13 per cent of all patients with chronic pulmonary suppuration develop abscess of the brain or meningitis. Our own figures closely approach his figures. Therefore if, say, 12 per cent of the cases of cerebral embolism are added to 10 per cent of the cases of malignant disease, in 22 per cent death is likely to occur, if all the cases of pulmonary suppuration are included. Of course, surgical measures can be employed in some cases of cerebral complications, some patients with abscesses of the brain recover after operation. Unless we discriminate as to what sort of case we are talking about and deal only with pulmonary suppuration in general, we shall find that the mortality rate is high regardless of the kind of treatment.

With these words of introduction, I should like to speak about certain specific matters brought up in this symposium. One is the question of treatment in cases of refractory chronic suppurations, particularly so far as it applies to treatment with the cautery. Many consider me an ardent advocate of this kind of treatment. This radical operation with the cautery should be performed only in the most refractory cases. We start, therefore, with cases which are bad surgical risks, cases which usually have resisted other forms of treatment, including simple drainage, sometimes thorocoplasty and other types of treatment. I am rather disappointed to find that other surgeons have not had the same satisfactory experience with this operation that I have had. I am particularly disappointed to find that the subject of hemorrhage is referred to so frequently. My own experience in these cases consists of a series of forty-five cases in which my associates and I have carried out a radical cautery operation such as I have described elsewhere.

In this series of forty-five cases, considerably more than 100 extensive cauterizations have been performed, I cannot say off-hand just how many. In only one case has there been troublesome hemorrhage. That occurred in a child, aged 6 or 8, who died of hemorrhage on the twelfth postoperative day, and who was found by the nurse early in the morning lying dying in a pool of blood. We have had hemorrhage in other cases, but there has never been any difficulty in controlling it. I think that in this case the hemorrhage could have been controlled if the patient had been an adult instead of a child, and if he had notified the physician or nurse that something was wrong.

If serious hemorrhage occurs during the time that the cauterization is being performed we either clamp the large vessel which is bleeding and ligate it, or, if that is not easily done, we pack and stop, and do not continue with the cauterization at that time. We have never found any difficulty in controlling any kind of hemorrhage from a vessel that we have encountered at this operation by the simple device of packing. We ordinarily leave the pack undisturbed for five or six days, then it is removed, and a clean pack is substituted. I should say, of course, that great precautions are taken at the time of removal of the first pack. Everything is made ready to put in another pack immediately in case hemorrhage should start again. We keep the lung packed tightly for ten or fifteen days. I prefer to carry out this procedure by easy stages, multiple stages, rather than to attempt to do too much in one step.

I feel that possibly one explanation of hemorrhage that occurs to other physicians who have performed this operation or followed this procedure has been that they have not been working through a wide enough exposure. I feel that it is essential to have a free, wide exposure. This is usually accomplished by the resection of three or four ribs at the first operation, then everything is before one's eyes and one can see everything that is happening in that area of lung tissue.

# THE EMPYEMA PROBLEM \*

AMBROSE L. LOCKWOOD, M.D.

TORONTO

There are few diseases that have perplexed the profession so generally since the earliest times as has empyema. Even in this advanced era of medical development, there is no agreement as to the treatment, as is evidenced by the various methods advocated, the persistent incidence of chronic empyema and the extreme variations in mortality incidental to treatment by various methods. Because during the several stages of the disease the patient requires the attention of those specializing in various branches of medicine, every effort should be made by the medical profession to recognize the etiologic factors in the condition, to be familiar with methods of avoiding it, to make an early diagnosis and thus control the course of the condition and, if possible, to determine a more routine method of treatment with the minimum of mortality. As a rule, the patient first comes under the care of the general practitioner, he is then referred to the medical consultant, the roentgenologist, the bacteriologist, the surgeon and the anesthetist and then back to the practitioner.

Hippocrates first recognized the disease. He advised intercostal incision or trephining of the rib for drainage. His treatise on the subject was as lucid as any that have appeared until recent years. The sound advice of Hippocrates was later neglected or forgotten. For centuries following the invention of the aspirating syringe by Galen, aspiration was employed. Because of the fear of admitting air to the pleural cavity and the dread of sepsis, free incision for empyema was not practiced from the time of Galen till that of Lister. Paget,<sup>1</sup> in his "Surgery of the Chest," says

As late as 1872 Bouchut published, as an instance of good profitable surgery, a case of empyema in a boy, aged nine, cured in 16 months after 58 punctures. In another case he punctured the chest, in 11 months, 123 times.

Tilly recorded a case in which he made fifty-six punctures. Gimbert made seventy-four punctures in nine months in a child, aged 1 year. Of forty-eight patients thus tormented, only six were saved. Of twelve patients under the care of Velpeau, not one recovered. Of fifty-eight under the care of Dupuytren, all but two died. Sir Astley Cooper complained that he never obtained a cure. Is it curious that with the establishment of free drainage again in Lister's time aspiration was abandoned until that great master surgeon, Murphy, adopted it? He also injected 2 per cent solution of formaldehyde and glycerin into the pleural cavity.

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\* From the Section of Surgery, Lockwood Clinic.

<sup>1</sup> Paget, *Surgery of the Chest*, New York: E. B. Treat & Company, 1897.



pneumothorax alone, and some have been well for five years without recurrence. They must be properly selected cases, of course. I do not want to go into this aspect too much. We have long felt that sinus disease was an important association of chronic pulmonary suppuration, and we regard the examination of nasal sinuses of just as much importance in the examination of a person with chronic pulmonary suppuration as the examination of the lung. We have had astonishing results, often we see spontaneous healing in advanced cases merely after the correction of suppuration in the nasal sinuses, this is particularly true in the cases of children.

I was much interested in Dr Kernan's report of his series of cases of bronchoscopy. So far as I know, only one other report has been published on actual results of bronchoscopic treatment in suppuration of the lung. That report does not concern any large series of cases, but is a report of only thirteen cases from the largest bronchoscopic clinic in the world, namely, the Jackson Clinic. I have been able to find only thirteen cases reported on the success of bronchoscopic treatment in pulmonary suppuration. Twenty-five per cent of the patients were reported cured, 30 per cent were reported unimproved and the rest improved.

It is interesting that bronchoscopy, according to Dr Kernan, is most effective in certain types of cases, notably the post-tonsillectomy abscess situated near the root of the lung. That type of abscess responds to treatment by rest in bed with postural drainage and heals spontaneously more easily than any other type of abscess. I think that is a point we must consider. I do not wish to imply that I condemn bronchoscopy. I think it has definite indications, but I think that we must remember that the cases which give the best results in bronchoscopy are the ones in which the abscess is most likely to heal spontaneously, excepting the cases associated with foreign bodies.

DR LIEBENTHAL. Dr Graham's report simply substantiates what I said about discharging patients who are not absolutely cured—those who have uncured abscesses, those who have bronchial stomas and those who have any signs that the lung is not well. They may have recovered from the operation and have been clinically cured, but for a long time one cannot tell whether or not they will die from some condition that was connected with the original disease for which they sought treatment. Dr Graham has said this himself. I am not objecting to treatment with the cautery. On the contrary, I think that if properly performed in suitable cases the results are undoubtedly good. We know that Graham's results have been excellent. When he says that 10 per cent of the patients would die of cerebral abscess in any event, it must be admitted that we cannot know which 10 per cent they are. But I maintain that with operations of a kind in which the diseased part of the lung is removed beyond ligatures, cerebral complication must be rare. I have not seen it in a single case in the lobectomies I have performed. It will take us a very long time to find out whether or not cerebral complication is more common after burning.

Dr Graham says that two patients died of pneumonia from one to one and a half years after operation. I would be more convinced if they had died of some disease not connected with suppuration of the lung. They died of a lung disease, and I cannot help thinking that these may have been connected with the original pulmonary infection.

I do not remember that I have ever operated to cure a bronchial stoma. I agree with Dr Graham that when the cause of the bronchial stoma is no longer present, it will be difficult to keep it from closing. I shall report a case at

When aspiration is being performed, just before the needle is withdrawn, a little alcohol or 1 per cent mercurochrome-220 soluble is introduced into the needle with a syringe, and the needle is slowly withdrawn so that the antiseptic escapes into the tract and prevents infection which is troublesome, particularly if operative intervention through the same site is necessary later

#### CHRONIC EMPYEMA

Chronic empyema must be considered the result of an improperly treated acute empyema. If the cavity is present from six to eight weeks after the development of the disease, for practical purposes it is classed as a chronic empyema. Whittemore<sup>7</sup> aptly indicated the reasons why an acute empyema becomes chronic when he said that "it is either a neglected case, and has not received surgical attention when it should have, or it has been badly operated on, or the after-care has been poorly managed." Lack of cooperation on the part of the patient contributes to an unfavorable result.

There should not be undue haste in dealing radically with the cavity. Radical operations should be decided on only after the exact location, size, nature and accurate ramifications of the cavity have been determined, and then only when, after a thorough trial with the Carrel-Dakin treatment, the application of various dyes (Kellar), blowing exercises and suction and other methods, the cavity is not being reduced in capacity. Then radical operative intervention should not be delayed, if the patient's general condition has improved as much as can be expected, with the thorax still open, and if the patient's resistance generally is such that he will stand the operative reaction to be expected.

The factors contributing to persistent drainage in these patients are

- 1 Necrosis of the bone or cartilage adjacent to the sinus
- 2 A drainage opening that is not dependent
- 3 A foreign body within the cavity
- 4 Extensive fibrosis about the sinus tract that will not permit healing
- 5 Multiple pockets within the cavity that do not drain dependently
- 6 Such extensive thickening over the visceral pleura that the lung cannot possibly expand farther
- 7 Adhesions to the mediastinum, diaphragm or pericardium
- 8 Tuberculosis, syphilis, pyocyanus infection and actinomycosis

In all cavities that will contain more than 3 ounces (89 cc), it is the practice in the Lockwood clinic<sup>8</sup> to endeavor to expand the lung to the wall of the chest rather than to collapse the wall of the chest to the lung. In most cavities under 3 ounces (89 cc), especially if peripherally placed,

7 Whittemore Personal communication

8 Lockwood, A. L. The Scope of Thoracic Surgery, Arch Surg 10 280 (Jan) 1925

# COUGH

## ITS ACTION ON MATERIAL IN THE TRACHEOBRONCHIAL TRACT EXPERIMENTAL STUDY \*

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If one were asked the question "What is the function of cough?" the reply would probably be that it is to clear the respiratory tract, of either an irritant or a block to the free passage of air in and out of the tracheobronchial tree. Thus, the general conception would be that the act of coughing results in an expulsive force which tends to drive whatever substance is producing the irritation, or block, up and out of the respiratory tract. The purpose of the experiments under consideration was to determine, whether or not this was the sole result of the act of coughing on material in the tracheobronchial tree. For, it had occurred to one of us,<sup>1</sup> as doubtless to many others, that cough, under certain circumstances, might actually be the means of spreading the material which produced the irritation deeper into the finer ramifications of the pulmonary tree rather than of expelling it.

### PHYSIOLOGIC CONSIDERATIONS

While cough may be voluntary, it is generally a purely reflex and unconditioned response to local irritation in the air passages originating nerve impulses which are transmitted by afferent fibers in the vagus nerve. The efferent portion of the reflex arc is completed through motor nerve fibers innervating the intrinsic and accessory muscles of respiration. The excitation of these motor nerves results in a contraction of the muscles involved. The abdominal muscles contract, bringing about an increase in intra-abdominal pressure which is transmitted through the semirigid diaphragm into the thoracic cage. The intercostal muscles, aided by the abdominal and lumbar groups, tend to elongate the bony frame-work of the thorax and thereby markedly decrease its average diameter. The accompanying contraction and fixation of the diaphragm further narrows the chest cavity and completes the contraction of the boundaries of the thoracic cage, except for the upper segment represented by the neck. This is held rigid by the long muscles of the neck, leaving only the exit through

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\* This article appeared also in *Am Rev Tuberc*, August, 1927

1 Archibald, E. *Am Rev Tuberc* 15 564, 1927

absorption of the fibrinous barrier between the alveoli, and that there are more failures in obtaining complete expansion following decortication in patients operated on with cavities of from six to eighteen months' duration than in those with cavities of longer duration

Delorme,<sup>11</sup> having noted the degree of expansion possible in lung tissue in old empyema cavities examined at autopsy, operated on a patient in 1894. He reported little trouble with the actual decortication itself, but the patient died of shock and hemorrhage. American surgeons did not take kindly to the procedure, and in 1913, Beckman<sup>12</sup> could find only twenty-four cases reported in the literature, all the operations were performed by three operators. Ransohnoff,<sup>13</sup> after the experiences of Fowler and Delorme, modified the operation, making multiple incisions at right angles. There are a percentage of patients in whom the pleura will not strip, and the methods of Ransohnoff must be resorted to although expansion is never so complete. Beckman's advice "to attempt decortication first and, when it fails, to try other methods" should be followed. It has been our experience, however, that a minor preliminary operation to secure adequate drainage and permit proper irrigation according to the Carrel-Dakin method has been necessary in over 9 per cent of patients who have come under our care in the chronic stage of the disease. Robinson<sup>14</sup> stated that nine tenths of his patients required such a preliminary operation.

We have so modified our method of decortication that we rarely have any trouble at the time of operation or after from the operation per se, but it must be borne in mind that to get the most complete result from a decortication, the incision must be hermetically sealed so as to establish a negative pressure and maintain the reexpanded lung in expansion. This is not always easy in cases of long standing in which the patients have had repeated operations with removal of tissue and loss of elasticity of the tissues about the scar and in the presence of extensive scars with a poor blood supply. If the incision is hermetically sealed, the patient must be closely watched for the development of intrapleural pockets, and repeated aspirations must be performed to keep the thorax free from fluid.

On the whole, however, a certain amount of the wall of the chest has had to be removed in most instances, so that in addition to methods of expanding the lung a means of dealing with the wall of the chest itself must be considered to allow adequate drainage, inspection and manipula-

11 Delorme. *Seventh Congress de Chir. Paris, 1893*

12 Beckman, E. H. *Decortication of the Lung for Old Empyema*. *North-west Med.*, vol. 6, 1914.

13 Ransohnoff. *Ann. Surg.* **43** 502, 1906.

14 Robinson, Samuel. *The Treatment of Chronic Nontuberculous Empyema*. *Surg. Gynec. & Obst.* **22** 557, 1916, reprinted by the Mayo Clinic **7** 612.

Thus, two *a priori* factors whereby cough may actually spread material deeper into the pulmonary tree rather than merely expel it, may be considered, namely (a) the inspiratory rush of air and (b) the expiratory effort

#### THE INSPIRATORY RUSH OF AIR

It is obvious that a single cough does not always clear the pulmonary tree of the irritating substance. Therefore, it may be assumed that in many instances this irritating substance is acted on by the increased inspiratory rush of air which follows cough and which may possibly carry it, or a portion of it, on into the finer bronchioles or even into the alveoli (fig 1). In case the entire mass has been transported by the inrush of air, either in toto or in a subdivided state, the situation is one in which a substance which originally was in a sensitive area of the pulmonary tree is now in a region where its presence does not produce a stimulation to cough. Even if most of the substance is subsequently

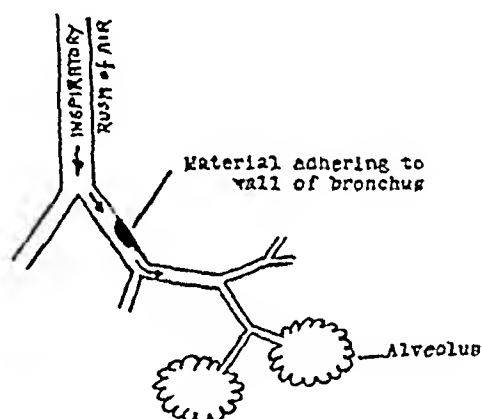


Fig 1—Showing how the increased inspiratory rush of air that follows cough strikes substances in the tracheobronchial tree and may spread them into the finer alveoli

expelled by cough initiated elsewhere, it is still clear that a chain of events takes place whereby particles may be transported, by one phase of the act of coughing, downward into the finer ramifications of the pulmonary tree, where they may come to rest. If, now, the material is of an infective nature, a pathologic process may be initiated

#### THE EXPIRATORY EFFORT

Since the advent of the use of opaque substances for the roentgen-ray and fluoroscopic visualization of the pulmonary tree, it has become possible to witness what actually occurs during cough, and several reports of the spreading action of cough have appeared in literature. For example, Ameuille<sup>4</sup> injected iodized oil 40 per cent into the right lower

<sup>4</sup> Ameuille. Injection transparietale de lipiodol dans une cavité pulmonaire, production sous l'écran du phénomène de l'embolie bronchique, Bull et mem Soc med d hôp de Paris 98 791, 1924

## CONCLUSIONS

The closure of a chronic empyemal cavity is a mechanical problem. The general health and resistance of the patient must be appreciated. The exact size and ramifications of the cavity must be determined by roentgen-ray examination and by direct inspection and measurement of the cavity. Adequate drainage must be secured. Carrel-Dakin irrigation must be carefully and thoroughly carried out so that every surface of the cavity is bathed in the fluid. Blowing exercises must be begun. Every effort must be made to build up the general health of the patient, and, finally, with proper appreciation of the risks, difficulties and sequelae of the operations and the resistance of the patient, the lung must be expanded and the wall of the chest collapsed, so as to obliterate the cavity. Multiple small operations safely carried out reflect the sound judgment of the surgeon. A patient should not die in the chronic stage of the disease, except from tuberculosis, actinomycosis or lardaceous disease in the late, neglected type of case.

Postoperative death of patients with chronic empyema gravely reflects on the surgeon. Robinson states that "An operative fatality in chronic empyema is inexcusable." I agree with him.

## ABSTRACT OF DISCUSSION

DR HOWARD LILIENTHAL, New York. I have been greatly interested in these constructive papers.

Dr Crowe's paper is an epoch marking contribution, in it he tells how he showed experimentally in the dog, an animal in which it is especially difficult to produce pulmonary suppuration, how the production of a sinus suppuration was followed by typical abscesses of the lung. The specimens were convincing and the paper most instructive.

Dr Crowe spoke of chronic abscess of the lung caused in this way, I should say that such an abscess would become chronic only after it had been an acute abscess. I cannot conceive of an abscess of the lung as being chronic from the beginning. Perhaps I am a stickler for words, but I would suggest some change in the terminology, perhaps calling it a slowly progressive abscess.

As regards hemorrhage as a cause of death in dogs, I do not know what the experience of others has been, but in my observation hemorrhage has been an extremely common and dangerous complication of gangrenous abscesses of the lung, especially in bronchiectatic cases. The process is a true spreading gangrene with ulcerations in the vessel walls, not only of the pulmonary but of the bronchial system of arteries. I am sure that these hemorrhages occur because of the spreading gangrene, the destructive inflammation.

I should like to hear the opinion of others as to their experience. I think that I have had more deaths from hemorrhage in cases of suppuration of the lung than I have had in cases of tuberculosis.

I think that Dr Crowe mentioned something about massive collapse. I do not believe massive collapse of the lungs is always inspirational. It has been difficult to prove because so few of these patients die, but recently a case was

sputum into which the oil was injected by means of a very fine needle and syringe in the proportion approximately of one part of oil to two of sputum.

The experiments must further be subdivided into (a) instances in which no attempt was made to induce cough, (b) instances in which cough was induced by mechanical stimulation of the posterior pharyngeal wall and (c) instances in which in addition to the mechanically induced cough an artificial block to the expiratory force was present. This block was produced by compression of the upper tracheal segments through the pretracheal tissues with the fingers.

The method of introduction consisted, first, in general ether anesthesia sufficient to abolish cough but light enough so that cessation of anesthesia almost immediately brought about a return of the cough reflex. The introduction of the iodized oil alone or the iodized oil-sputum emulsion was carried out in

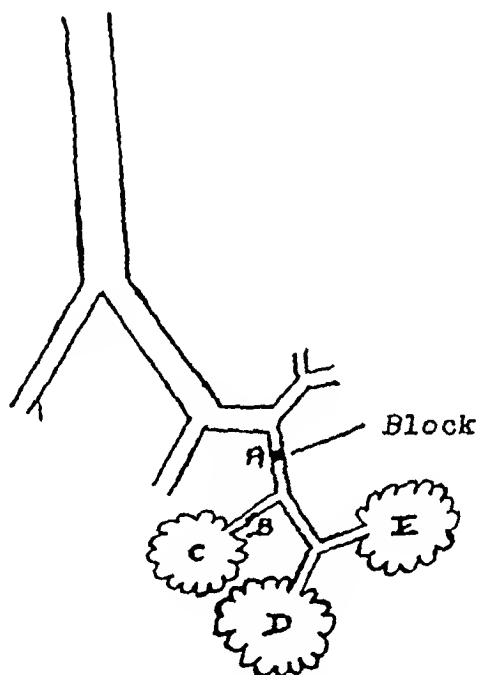


Fig 2—Showing mechanism whereby material may be driven distally by cough or spread into neighboring alveoli when a block exists proximal to the material in question. Thus, it is assumed that a block exists at *A*, then the material *B* approaches *A* during cough and immediately afterward is carried distally toward or into the alveolus *C*, or possibly into other alveoli distal to the block, such as *D* or *E*.

2 cc amounts by the intercricothyroid route after first determining the position of the needle in the trachea by the free aspiration of air into the syringe. It was necessary to perform a tracheotomy for the introduction of the thick sputum masses which had been injected with the iodized oil. This was done through a tight fitting tracheotomy tube with the cannula in place, so that all respiration went on through the tracheotomy opening and none by way of the pharynx. Moreover, because these large masses of sputum tended to block the trachea, it was found advisable to introduce them at the onset of the inspiratory effort, so that they would surely be carried as far as the bifurcation and thus allow at least partial respiration to proceed. When narcosis was established, the animals, fastened on an animal board, were

infection along that route by way of the lymphatics has been clearly demonstrated by many, yet it has so often been overlooked that it seems to me wise to call attention to it again

There seems to be little doubt that emboli cause infarctions with subsequent infections. It seems proved that aspirations from various places in the upper respiratory tract cause bronchopneumonia that may precede bronchiectasis.

The differentiation made not only during clinical examinations, but during autopsy seem important. In bronchopneumonia the areas of infection spread to the tissues of the lung immediately surrounding the bronchi. In lobular pneumonias patches of infection are seen in the parenchyma of the lung that may or may not be confined to the region of the bronchi.

Then there are cases of pneumonitis, if one wishes to call them such, which are diffuse infections spreading along the trabeculae and subpleural planes in a manner similar to that in which infections spread in other parts of the body. There are so many cases that follow operations performed under local anesthetics, so many cases in which there have been infections of the lung due, I think, to seasonal variations in the types of infections, and so many that show infections that apparently have started in the lobular or in the parenchymal part of the lung without explicit juxtaposition to bronchi or absolute evidence of their origin by vascular route, that one is forced to consider that antigen gains entrance to the lung by the lymphatic route to act as a predisposing if not exciting cause.

It seems to me important that to keep one's mind open to the distribution of these infections by all three routes—blood, bronchi and lymphatics—instead of being too sure that any one of these routes is responsible for the spreading of all infections.

DR. WILLY MEYER, New York. The various speakers have covered the entire field thoroughly. Regarding etiology, I believe that when the question of abscess of the lung being due principally to embolism came up about two years ago, many who had observed these cases carefully, said to themselves "Surely many of these cases are due to embolism." How can it be different? A septic embolus driven into the pulmonary artery or its branches must produce infection of the lung—but from what we have seen, observed and learned in the course of many years, it seems improbable that embolism should be the principal cause of abscess of the lung.

First, let us consider the aspiration that we have seen in so many instances following tonsillectomy. I know that up to this day many laryngologists insist that it is not the aspiration of blood and mucus accumulating in the pharynx during the operation which caused this terrific consequence to the patient, but that it is embolism. To the majority of us that does not seem to be the real explanation.

Furthermore we had observed abscess of the lung following aseptic operations performed under general anesthesia, for instance after an ovariectomy also after an operation for strangulated hernia, performed by other surgeons. In both patients perfect aseptic healing occurred, and yet an abscess of the lung followed, in one instance complicated by a sacculated empyema.

How could that be due to embolism? There was aspiration during general anesthesia, and as the patients aspirated some of the contents of the stomach it was fortunate that the stomach had been kept empty before operation and that far-reaching gangrene of the lung did not follow.



material failed to enter the trachea, having been injected by mistake into the pretracheal tissues. In four instances in which it was impossible to elicit cough within the allotted time, anesthesia was stopped and the animals were taken as controls of the rate of expulsion of the oil when cough had not been induced. In the eleven other instances, satisfactory cough was obtained, in five cases without tracheal compression and in six with compression. In some only one strong cough, while in others as many as twelve successive coughs were induced. All the animals coughed more or less strongly on coming out of the anesthesia, and several were observed to swallow material which had apparently been coughed up. Roentgenograms taken on successive days showed the length of time the opaque substance remained in the lungs in sufficient quantity to cast a shadow by roentgen ray. A comparison of the roentgenograms showed that, on the average, infiltration of the pulmonary tree with the opaque substance took place more rapidly and more completely with cough than without, and this observation was still more pronounced with cough plus tracheal compression. Figures 3, 4 and 5 are examples of the degree of penetration under these three conditions, all taken three minutes after the introduction of the oil, and in figures 4 and 5 within one minute after cough had been induced, in the latter case with tracheal compression. Moreover, it was noted that the oil tended to remain longer in the lungs of those animals in which cough had apparently caused a deeper penetration, and that it remained longest in those instances in which tracheal compression had been employed. This was probably due to the fact that with induced cough, and especially with cough plus tracheal compression, a larger quantity of oil reached the alveoli than was the case when the flow of the oil was uninfluenced by artificial factors.

Figures 6, 7 and 8 correspond with figures 3, 4 and 5 in that they are subsequent roentgenograms of the respective cats. They illustrate comparatively the amount of iodized oil remaining in the lungs. Thus, figure 6, taken one day after figure 3, shows practically no iodized oil remaining in the lungs, cough had not been induced in this cat. Figure 7, taken four days after the introduction of the oil in a cat in which cough had been induced, shows a considerable quantity of the oil still in situ, while figure 8, taken twenty days after the introduction of the oil, shows the greatest quantity of the oil remaining after the longest period. It is, of course, to be understood that the amount of oil present and the length of time it remained in the lungs differed somewhat at every trial, but the illustrations demonstrate fairly the type of variations noted under given experimental conditions. The actual presence or absence of the oil in the finer bronchioles and alveoli was further demonstrated in every case by frozen sections stained with scarlet red or sudan III.

in whom spontaneous healing will occur, and we should not wait and trust to luck and posture with general treatment, but we should refer the patient to the bronchoscopist. If the bronchoscopist cannot accomplish the desired result, then I believe we should resort to artificial pneumothorax, unless the patient requires surgical measures. Personally, I would not start with artificial pneumothorax.

Speaking of conservative surgery, I think, that the establishment of a permanent opening into a smaller or larger bronchus is one of the best conservative treatments in cases of infection of the lung. We called this method lung lip fistula in order to express the idea that it is not expected to heal quickly, others have called it bronchostomy. In a number of instances these patients improved materially, the fistula later healed spontaneously or almost completely, and it did not bother them. If this does not happen, I agree with Dr. Lilienthal that after a certain time one should try to close the fistula. The majority of patients are disinclined to have this done. They say, "I am perfectly well, why should I bother about it?" We all have observed that spontaneous closure occurs not so infrequently. These patients should not be left to themselves on account of the possibility of future hemorrhage.

A few words more about the remarkable case of prompt disappearance of acute pneumothorax. I also believe that if the lung collapses the explanation of the occurrence of a hyperemia of the collapsed lung is probably correct, as Cloetta has maintained. It was explained that sometimes chronic hyperemia acts so quickly also after extrapleural thoracoplasty in the tuberculous patient, that it almost forces the conclusion that it is principally responsible for the cure of some of these patients in such a brief time.

Dr. Pickhardt's presentation of the unresolved pneumonia has shown that we can prove definitely by follow-up that many of the cases which were called chronic pneumonia represent a surgical infection or condition. Two years ago, I reported a case before our association in which the condition was diagnosed first as chronic pneumonia. We might just as well have called it unresolved pneumonia or carcinoma. I would like to repeat here that diathermy, so far as therapy is concerned, had a most remarkable effect. The fever that had been present for weeks disappeared after a few applications so that the attending physician whom I had called in consultation rejoiced that his advice had had such a splendid result. I, too, was pleased, however, it was shown that at the bottom of the cause of trouble was a malignancy of the upper lobe which gradually became more conspicuous. The accompanying chronic inflammation had been beneficially influenced by diathermy.

I have one more remark to make with reference to the so-called massive collapse first described by Dr. Scrimger. Personally I was totally bewildered at first. I wondered what could be the cause of the sudden collapse other than a clogging of the bronchus. In thinking over what we had seen in animal experimentation in former years, viz., that the tying of the branch of the pulmonary artery alongside the bronchus produces rapid shrinkage and cancrification of the lobe by interrupting its physiologic work, it seemed plausible that an aseptic embolism might eventually act likewise. However the spontaneous disappearance of the condition in some instances and still more the fact that prompt bronchoscopy with aspiration of a large amount of thick secretion from the respective bronchus quickly aborted some of these cases proves that actual obstruction of the bronchus produces the acute atelectasis of the pulmonary parenchyma which Dr. Scrimger called as the first acute massive collapse.

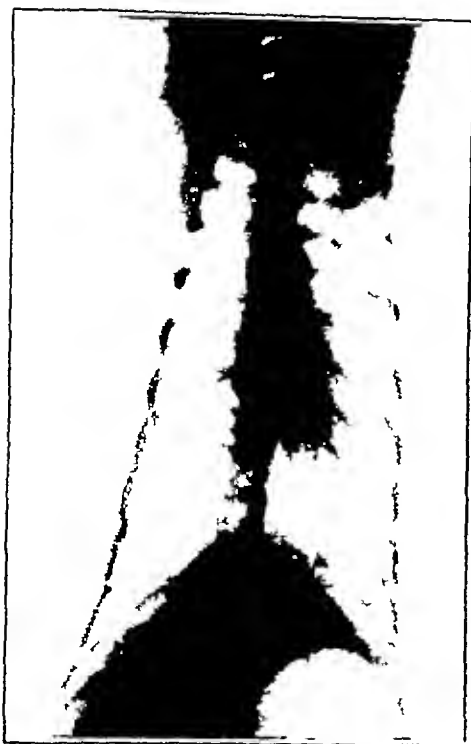


Figure 6

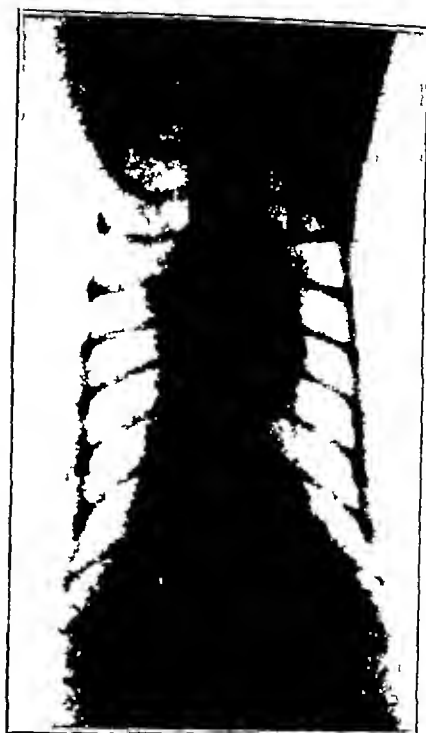


Figure 7

Fig 6 (cat 20) —Taken one day after figure 3 There is little increased density, practically all of the iodized oil having been expelled

Fig 7 (cat 15) —Taken four days after figure 4 Some iodized oil is still present as evidenced by the increased density in both lower lobes, especially the right

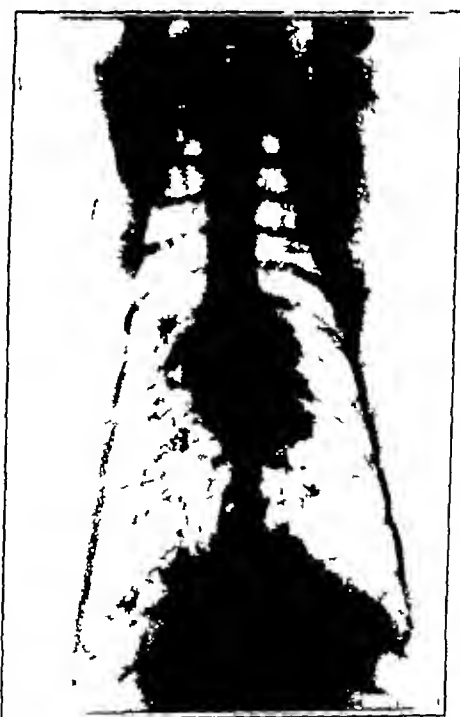


Fig 8 (cat 11) —Taken twenty days after figure 5 A large amount of iodized oil is still present, apparently in the finer bronchioles and alveoli, as evidenced by the diffuse and fine shadows cast

an abscess may be difficult to find by thoracotomy, and the danger of hemorrhage from adjacent large vessels is considerable. It is most favorably situated for adequate drainage through an adjacent large bronchus. A peripherally situated abscess draining imperfectly through a relatively long sinus connecting it with a main bronchus, especially if it is large and shows a fluid level, in my opinion, should be drained. The nearest exit for the pus is through the wall of the chest. Enlarged cavitation, hemorrhage, and all the train of sequelae of chronic septic absorption result from unduly prolonged expectant treatment in such cases, and the difficulties and dangers of operation in the chronic stage are greatly multiplied. I believe that drainage should be instituted in all peripherally situated abscesses that do not present unmistakable evidence of healing during a period of almost two months of conservative or expectant treatment. Treatment with arsphenamine is indicated in all cases in which spirochetes are found in the sputum.

Chronic abscesses presenting an epithelialized cavity with multiple bronchial fistulas require wide open drainage and cautery to destroy the epithelial lining; some eventually require further plastic surgical measures.

Cases of multiple abscess are the most difficult of all. In my experience, cautery lobectomy is the most effective.

In bronchiectasis, compression therapy by phrenico-exercise, pneumothorax collapse and thoracoplasty, should in my opinion be given first consideration. If such treatment is carried out early in unilateral cases of the peripherally localized saccular type such as can be differentiated by the contrast mediums, improvement, approximating a cure may, I believe, be expected in the majority of cases. Later, lobectomy can be performed with relatively much less risk than primary lobectomy in patients not sufficiently benefited. The marked and extensive fibrosis that results from the thoracoplasty, if not curative, will greatly facilitate the closure of the bronchial stump following either eradication by cautery or lobectomy.

DR JOHN L. YATES, Milwaukee, Wis. I shall consider the problems of intrapulmonary suppuration from a biologic aspect. Infections in and on bronchopulmonary structures are inevitably so frequent as to be virtually constant. Insusceptibility or susceptibility to infection, whatever the type of the micro-organism, recoverability or irrecoverability from infection after it is established, healing or failure of healing of lesions are traceable to strength or weakness of the powers of resistance, defense and repair. Correct definitions of these interlocking processes which control our destinies are imperative, because they are the foundation of therapy.

Resistance is provided by responses of fixed tissue cells adjacent to infection, reinforced by the cellular and noncellular elements delivered in the blood. Adequate resistance promptly suppresses invading micro-organisms without recognized signs or symptoms, and there is insusceptibility. Degrees of inadequacy of resistance impose corresponding grades of susceptibility.

Defense is developed after infections become established through the responses of fixed tissue cells within the local lesion strengthened by the cellular and noncellular elements delivered in the blood. Adequate defense promotes undelayed recovery with the least destruction of tissue. Inadequate defense intensifies and prolongs immediate disabilities, and destruction of the tissue is correspondingly greater.

Repair begins with the destruction of tissue and is continued until healing is complete, until obstructed by cicatrices and relative ischemia or until terminated at death. Repair consists of the responses of fixed tissue cells sup-

head and chest of the patient inclined downward. Postural drainage, in this sense, at the time of operation will aid in the immediate elimination of a majority of the fluid pus escaping from cavities.

This action of cough may likewise be the explanation of the manner in which vomitus and material from the buccal cavity reaches the alveolar spaces. Aspiration probably carries the material into the trachea and larger bronchi, but it is difficult to conceive that aspiration alone could



Figure 9



Figure 10

Fig 9 (cat 13) —Taken after injection, through a tracheotomy tube, of thick tenacious sputum, which had been injected with iodized oil. The masses are shown fairly intact.

Fig 10 (cat 13) —Taken shortly after figure 9 and immediately after cough with closure of the tracheotomy tube. No great change in the position nor spread of the injected masses of sputum is shown.

take the material as far as the alveoli, where it would have to come to rest in order to produce postoperative pulmonary infection. It appears far more likely that cough expels most of the fluid material after it has been aspirated into the trachea and larger bronchi, but forces some of it into the alveolar spaces.

When suitable paralysis of the diaphragm and measures to improve the quality of the blood are used as introductory procedures in combating broncho-pulmonary inflammation that does not subside spontaneously, they alone may promote healing. If they fail, subsequent intervention is less hazardous and often less extensive operations are required. If the paralysis be made transient, from three days to three months according to the method employed ultimate recovery is without disability. If recovery or motion of the diaphragm proves to be disadvantageous and a quiescent process is reactivated, a permanent paralysis may be required.

One fact, not as yet accepted, has been established. Collapse of the lung caused by the abolition of intrapleural negative pressures and pulmonary compression produced by pressures exceeding that of the atmosphere, not only impose a restriction of blood supply to the lung, but also increase cardiac labor. Relative anemia reduces resistance, defense and repair. Excess cardiac effort narrows the margin of safety. Collapse is rarely needed and is attained by complete resections of all ribs. Compression is seldom justified.

DR. KENNON DUNHAM, Cincinnati. The symposium has been much more stimulating to an internist than I imagine it might be even to a surgeon. Nothing has been more striking than the experiments of Dr. Crowe, by which he placed infectious material from the teeth and the sinuses in the bronchi and produced abscess of the lung.

It is common for clinicians to note bronchiectasis, chronic bronchitis, bronchopneumonia and even abscess following sinusitis.

The close relation of the upper and lower air passages has been shown by a recent study of 700 patients sent to the Diagnostic Center of the United States Veterans Bureau in Cincinnati, and which soon will be presented by Dr. Skavlem and me.

The condition in the 700 patients had previously been diagnosed as some chronic disease of the lungs. Tuberculosis was the most common cause but 164 cases of chronic nontuberculous infections of the lung were reviewed in the series and 128, or 79.29 per cent. showed infection in the upper respiratory tract. Influenza, gas exposure and lesions of the heart accounted for most of the remaining 20 per cent.

Chronic infection of the ear should always suggest chronic sinusitis and the necessary examination should follow.

It is difficult to interest rhinologists in chronic sinusitis which does not cause symptoms in the head. Such lesions cause serious infections of the lungs. This society needs specialists in diseases of the nose and throat who will study and work with us, men who are studying the whole respiratory tract. Dr. Mullen, formerly of Colorado Springs now of Cleveland is such a man. He has done excellent research work along this line. He has proved that India ink can be carried from the antrum to the lungs and that the lymph nodes at the root of the lung are infected. He has not proved this transmission to be wholly through the lymph stream.

Infection from the teeth and sinuses can be directly aspirated into the bronchi. It is well that our surgeons are doing much to protect this route against infection.

The blood may also be infected pass to the right side of the heart and directly to the lungs, where the capillaries slow down the circulation and the white blood cells get their opportunity to attack the infection.

The system is better protected through the lymphatic stream.

Here the lymph chains act as natural barriers. These may be overpowered and the infection may reach the general circulation. Because the cervical chain

## ABSTRACT OF DISCUSSION

DR EVARTS A GRAHAM, St Louis I think all these fundamental considerations such as cough that have been taken up from time to time before this association are of the utmost importance, because any fundamental observation, of course, is of much more value than merely detailed observations relating to particular features of particular subjects. A number of points in Dr Archibald's paper interested me greatly. One point of practical importance that has come up in my own experience concerns the question of roentgen-ray interpretation after the use of iodized oil. I feel that since iodized oil is now, apparently, an accepted agent in the diagnosis of pulmonary conditions, the possibility of its having been used must always be considered in the roentgen-ray interpretation of films of the chest. What I mean more particularly is this. Recently I had a patient with pulmonary suppuration in whom iodized oil was introduced, pulmonary suppuration was confined to one lobe. Two months after the introduction of the iodized oil, the other lung on roentgen-ray examination seemed to be studded with extensive tuberculosis. That is to say, the plate mimicked accurately an extensive tuberculosis involving both lungs. As a matter of fact, the man was perfectly well at that time, and did not have any symptoms, not even cough. What evidently happened was that the iodized oil was scattered through both lungs, probably by coughing, as Archibald brings out. Unless the physician knew that iodized oil had been injected, if he had merely seen the plate, he would have been tempted to make the diagnosis of extensive tuberculosis in a person who was not at all tuberculous.

There are other dangers of cough which Dr Archibald did not mention. These are of practical danger to us as surgeons. I have seen an abscess of the lung rupture spontaneously during the course of operation under local anesthesia, as a result of violent coughing. Several times I have also seen pleural adhesions torn as a result of violent coughing. Several times, after suturing a lung to the wall of the chest in cases of pulmonary suppuration I have had the unpleasant experience of having these sutures torn away as a result of coughing during the next two or three days. Because this has happened to me, I have made it a rule to attempt to abolish the cough reflex as much as possible during the time in which I am attempting to create pleural adhesions. For that reason, it has been my practice to keep the patient under the influence of morphine for a period of days in order to diminish the cough as much as possible and thus to avoid tearing the adhesions. I am trying to create

Two other points that interested me concern the origin of the cough reflex and the spontaneous disappearance of cough reflex. First, in the series of experiments reported on abscess of the lung in dogs, Dr Allen found that for some reason some of the dogs coughed and others did not, regardless apparently of the location of the abscesses. Why some dogs coughed considerably during the whole progress of the abscess and other dogs seemed not to cough cannot be explained at present. In cases of bronchial fistula recently established, I have noted repeatedly (and this observation has been made by many others, for I have heard Dr Lilienthal speak of it a number of times) that the cough reflex from a bronchus of even considerable size will disappear over a period of time. I have made observations on a considerable number of patients. Soon after the establishment of the fistula, there will be an active cough reflex which can be produced easily by probing of the fistula. After possibly a couple of months or so, this cough reflex may have entirely disappeared, so that one can do almost anything inside of

localized acute pulmonary inflation with a foreign body, but I have not observed this type of disturbance in other than cases in which a foreign body was present. More commonly, irrespective of the cause, there are physical signs indicating partial or complete collapse of that part of the lung supplied by the occluded air passage. Roentgen-ray examination may afford such direct evidence as the shadow of a foreign body, but indirect indications of bronchial obstruction are more often obtainable and consist of changes which may be interpreted as due to pulmonary inflation or to collapse of parts of the lung supplied by the affected bronchus. Occlusion of a primary bronchus or one of its branches is so commonly associated with significant physical and roentgen-ray symptoms that their absence is to be regarded as evidence against bronchostenosis affecting these regions. Experience, however, is not sufficient at present to justify the belief that occlusion of the larger bronchi can with certainty in all cases be excluded by these means, and disturbances of the smaller bronchial branches fail to give significant symptoms. It seems desirable, therefore, that practically all patients with localized suppurative lesions be examined by bronchoscopy.

Dr Kernan is to be congratulated on his favorable results with bronchoscopic treatment. His twenty-nine "cures," 42 per cent, in sixty-eight patients on whom three or more bronchoscopies were performed is strikingly in favor of this method on comparison with my series of 106 cases in which the patients were treated by rest and postural drainage and in which twenty-four, or 22.6 per cent, recovered when the duration of the illness was eight weeks or less. I should like to ask Dr Kernan what his bronchoscopic procedure was.

DR. LILIENTHAL. I think Dr Lord was mistaken. Instead of "bronchoscopy," as he understood it, the word was "bronchostomy."

DR. ROBERT MILLER, Baltimore. May I say a word about the papers of Dr Allen and Dr Crowe? These two papers represent excellent laboratory work. In relation to that of Dr Crowe, I found myself working on the same subject three years ago, and consequently am more or less familiar with its development. All of us went through a phase of doubt as to whether one could produce an abscess in the lung of a dog. Some of us were beginning seriously to consider the dog immune from this condition. I was much surprised at the extreme type of experiment.

Our experience was that if one partially resects two ribs in a dog and exposes the lung, deliberately cauterizes an area straight into the parenchyma of the lung, burns it out, devitalizes it, then places in the cavity a rough metallic foreign body large enough to irritate the walls of the cavity and closes both the wound in the lung and in the wall of the chest without drainage, healing by first intention always follows. With the wound firmly healed we tried to inject cultures of hemolytic streptococci. We localized the foreign body and knew we were placing virulent streptococci together with a foreign body in a closed cavity. This inevitably means an abscess in the human body but not in a single one of these dogs could we produce an abscess of the lung. Curiously enough, even under the conditions described if the dog was allowed to live, the foreign body was sometimes extruded from the lung and lay in the pleural cavity. Until one has tried to produce an abscess of the lung in the dog it is difficult to realize how much work this paper by Dr Crowe and that by Dr Allen represents.

I was interested in the remarks of Dr Hedblom regarding the treatment in early cases of bronchiectasis in the lower lobe. We have encountered several cases of this sort in Baltimore recently. The patients have all come from the internists with a diagnosis of either early bronchiectasis, small abscess, or the



The physical means to control the useless cough and also to make the useful cough less painful and diminishing its intensity consist in bandaging or, rather, encircling the thorax with wide strips of Lilienthal's elastikon. Even if the encircling band is tight, its elasticity will permit the patient to breathe with relative comfort. The importance of thus restricting cough and respiratory movements at the same time is, of course, of obvious advantage in thoracoplastic cases. Under physical means of controlling useless cough I must also mention the importance of urging the patient to lie on his affected side, even during sleep. He will thereby compress the affected lung in a measure, diminish the respiratory movements and, *ipso facto*, lessen the desire to cough. The posture treatment can be aided materially by the use of little pillows placed so as to enable the patient to maintain the most desired position with the greatest ease and comfort. When the cough, which I designated before as a nervous or habit cough, cannot be controlled by discipline alone, it is well to suggest to the patient that he make a sudden inspiratory effort, that is to say, inhale quickly and shortly when he thinks he must cough. This method of treating habit cough is often effective.

My own method of reducing the number of respirations and limiting them to the diaphragm during the waking hours, I believe, may be justly considered as another physical means to control useless cough. I explained this method in full at the last Washington meeting of this association in my address on the subject of "Medical Care of Thoracoplastic Cases."

The last method of controlling cough is by medical means. These are too numerous to mention here, so I will limit myself to speaking merely of a few. Plain water taken in small sips will help to control the merely irritating cough. Sodium chloride in rather large quantities taken with food will help when the expectoration is so tenacious as to make the ejection painful. The various alkaloids of opium are often resorted to in combination with expectorants, such as ammonium chloride, ammonium carbonate, balsams of peru and tolu, licorice, cherry laurel water and glycerine. However, the most efficient anti-cough remedy in my experience is heroin, and I mention this not without a feeling of regret. It has been my privilege to serve in three military departments of this country—the regular army, the U. S. Public Health Service and the U. S. Veterans' Bureau. In none of them is the use of heroin allowed, simply because it is thought that the dispensing of heroin might lead to drug addiction. I am willing to confess that I have prescribed it from the time when it was first put on the market, and I cannot recall a single case in which addiction to heroin developed, perhaps because I was exceedingly careful. The largest dose I have ever prescribed was  $\frac{3}{12}$  grain (0.005 Gm.) every four to six hours, with the direction to give less as cough subsides, and I have never written a prescription without the injunction to the druggist "Ne repetatur sine ordine." When heroin cannot be prescribed, codeine is the best substitute. Of course, surgeons have a right to resort to hypodermic injections of morphine after a thoracic operation to allay the cough, but I feel sure that their experience also is that such injections to control painful cough and to diminish hurtful succussions lead to morphinomania only in the rarest instances, if ever.

I present these suggestions, not in the spirit of criticism of Dr. Archibald's valuable contribution, but as a possible help in the management of the cough.

DR. FREDERICK T. LORD, Boston. Dr. Archibald's paper brings up for discussion an important and often perplexing problem as to the best treatment

not to be accurate, because in the case of the lung there is a constant inside pressure of 15 pounds (68 Kg) to the square inch through the air passages, but, provided there is no obstruction in the air passages, this pressure remains the same, whether the lung is expanded, collapsed or compressed and therefore this factor need not be considered. We must therefore come to the conclusion that the greatest amount of blood is found in the expanded lung less in the collapsed lung and least in the compressed lung.

In reference to Dr Eggers' paper, his observation was exceedingly interesting, and the words selective action forcibly bring out Dr Eggers' meaning. Of course, the pressure within the thorax cannot select one part more than another, there will be an equal amount of pressure on all parts of the lung, the reason why there is an effect on the diseased part is that the pressure is more effective there. That particular part, previous to the pneumothorax, is edematous, and there is some destruction of tissue. The lung in that particular portion has lost its elasticity, consequently, the pressure on that part will be more effective than the pressure on the normal part of the lung. If, on the other hand, the same portion had already undergone cicatrization, the supposedly selective action would not be observed.

DR WILLIAM LERCHE, St Paul, Minn. I should like to mention two cases of foreign bodies in the bronchi with results analogous to those that Dr Graham had in his experiments, namely, multiple abscesses. In one of the cases a pimento, in the other, bits of peanut, had become lodged in the bronchi.

DR. E. A. GRAHAM, St Louis. I shall try to be brief, although there is a temptation to speak a good deal on this long list of papers.

I was glad that Dr Lilienthal made the statement which coincides entirely with my own opinion about these cases, namely, that at the present time there cannot be any standardization of treatment in cases of pulmonary suppuration. Furthermore, results which are important in a symposium like this are of necessity applicable only to the type of cases which the author is thinking about when he makes his report. For example, I know that I do not operate in certain cases of suppuration of the lung when others do. I know equally well that I operate in certain types of cases when other surgeons perhaps would not operate.

Therefore, when we are speaking of pulmonary suppuration, I think each of us has a certain reservation in mind which it is often difficult to express and describe when one deals with patients treated by a certain method and other patients treated by other methods.

If all cases of pulmonary suppuration without regard to type or distinction are placed in one large group, the proposition must be faced at once that no matter what form of treatment is given or whether or not any treatment is given, the mortality rate will be high. Why is that true? One reason is that at least in the experience of Singer and myself, based on more than 300 cases of pulmonary suppuration, 10 per cent of the cases have been associated with carcinoma of the lung, it has not always been primary carcinoma but it has at least been malignant disease of the lung.

With the present unsatisfactory method of treating patients who have malignant diseases of the lung 10 per cent, if the series is large enough, will die no matter what is done for them. There is also a large percentage of patients with pulmonary suppuration, at least in our experience, who have cerebral embolism or cerebral suppuration or meningitis. Many of these patients have come to us with these features already developed.

# INFECTIONS OF THE LYMPH NODES OF THE BRONCHIAL TREE

WILLIAM LERCHE, M D

ST PAUL

The tracheobronchial lymph nodes, as described by Sukiennikow,<sup>1</sup> were briefly outlined by me in a recent paper.<sup>2</sup> The bronchopulmonary nodes, also described by Sukiennikow, are found mostly at the angle of division of the larger bronchi (fig 1). Miller<sup>3</sup> stated that the bronchopulmonary nodes and lymph follicles are rarely found beyond the third division of the main stem bronchi, but that lymphoid tissue aggregated in masses of variable sizes are found throughout the lung. The situation of these masses may be peribronchial, periarterial, perivenous or

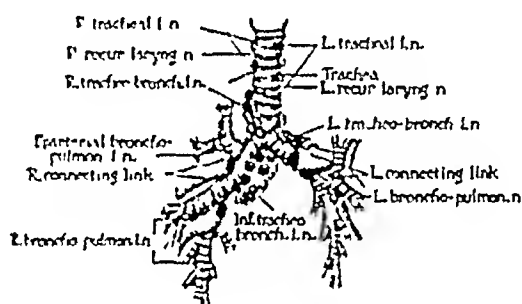


Fig 1—The tracheobronchial and bronchopulmonary lymph nodes (Sukiennikow)

subpleural. According to Miller, there are five locations at which lymphoid tissue is particularly found (1) where the radicles of the pulmonary vein arise from the pleura, (2) where veins arising from the distal end of ductuli alveolares join venous trunks situated on the periphery of the primary lobule (anatomic unit), (3) where veins arising near the place at which bronchi or bronchioli divide, join larger venous trunks which may be situated in septums of connective tissue, (4) at the distal end of the ductuli alveolares, and (5) at the place where

1 Sukiennikow, W. Topographische Anatomie der bronchialen und trachealen Lymph drusen, Berl klin Wchnschr, 1903, p 316

2 Lerche, William. Infected Mediastinal Lymph Nodes as a Source of Mediastinitis, Arch Surg 14 285 (Jan) 1927

3 Miller, W S. Studies on Tuberculous Infection. III. The Lymphatics and Lymph Flow in the Human Lung. Am Rev Tuberc 3 193 1919

Despite the fact that this type of operation has been reserved for the most refractory cases, essentially the cases of chronic suppuration that continue for periods of years, and despite the fact that many have been cases of multiple abscess and similar conditions, it seems to me that our results have been reasonably satisfactory. For example, in this series of forty-five cases, there have been three deaths which I would ascribe directly to the operation. One was the case of hemorrhage to which I referred. Two were cases of cerebral embolism, presumably, air embolism occurring during the cauterization, which resulted in instant death. In addition to that, however, there are four other patients who died while still in the hospital, I am willing to say that they died as a result of operation, but death occurred from four to ten weeks after the cauterization. They include (1) one death from acute cardiac dilatation sixteen days after cauterization, (2) one death from pyemia, in this case, abscesses were scattered throughout the body, if we had recognized that, we would not have kept on working at the lung, (3) two deaths from cerebral suppurative complications—meningitis in both cases.

Thus, seven patients have died in the hospital following this procedure, a mortality of 15 per cent. In addition, during the three years that we have been carrying out this procedure, we have learned that five other patients are dead. These patients died of various conditions not attributable to the operation of cauterization pneumectomy. Two died during attempts made elsewhere to close bronchial fistulas. Two other patients were said to have died of pneumonia. Possibly they had a recurrence of pulmonary suppuration, they died from a year to a year and a half after operation. In all, 25 per cent of these patients are dead, but 43 per cent are well, entire healing has occurred and bronchial fistulas or other conditions have not resulted. An additional 15 per cent of patients are free from symptoms and are back at their usual duties. Some of them are laborers who perform heavy labor, others are housewives, but the latter have bronchial fistulas. There are an additional 13 per cent on whom operation has been performed within the last six months who are well and free from symptoms, but I do not know yet what the results will be. There is one case, or 2 per cent, concerning which I have not been able to get a follow-up report. Twenty-five per cent of the patients are dead, but 73 per cent are known to be free from symptoms at the present time, most of whom are back at work earning their living and carrying on their usual occupations. Of the total number of forty-five cases in my own experience, there was only one death from hemorrhage.

Now a word or two about bronchial fistulas. I have a feeling that has been expressed once or twice at this symposium that bronchial fistulas had better be let alone. Some of the speakers do not agree, but in my own experience in the majority of instances, after bronchial fistulas have ceased to be of use they heal spontaneously. I think too much tinkering is done with them. I think the operation of closure of the bronchial fistulas is serious. In my cases fatal air embolism has occurred, which is as tragic as any death that could result from any operation of any type and still more tragic because one does not expect it.

I have been astonished to listen to the discussion on pneumothorax because I had thought that if there was one treatment which had been found to be effective in certain cases of suppuration of the lung, it was pneumothorax. It has been amazing to hear a controversial discussion on that subject. I did not bring our statistics along, but Singer and I have seen many patients with cases of acute abscess of the lung recover after the performance of

but communicate freely with each other. On the other hand, according to Miller, valves prevent the passage of any injection mass from the pleural lymphatics into the deep lymphatics of the lung, since the valves in the connecting vessels between the pleural and the deep lymphatics point toward the pleura. Therefore, when the normal drainage of the deep lymphatics of the lung toward the hilum is prevented, the flow may be into the pleural lymphatics. Miller suggested "that this arrangement of the valves, probably explains why tubercles may be found in the pleura and not in the deeper part of the lung." It also probably explains the formation of acute nontuberculous abscess in this locality. Valves pointing toward the hilum have been found in the main trunks draining the pleural lymphatics and also in the lymphatics about the pulmonary veins near the hilum. The lymph from the lungs, the bronchi and the lower part of the trachea and its bifurcation, as well as from the larger part of the pleura, is received by the tracheobronchial nodes. The lymphatics from the pleura of the inferior half of the lower lobe according to Cunningham, pass through the ligamentum pulmonale and drain into the preaortic lymph nodes.

There are two routes by which micro-organisms can enter the area drained by the tracheobronchial nodes. 1 They may be carried into the lower respiratory passages by inhalation, penetrate the epithelial lining and be conveyed to the tracheobronchial nodes by the lymphatics. Rogers<sup>6</sup> observed that seven days after guinea-pigs had inhaled tubercle bacilli, by being sprayed with an emulsion of tuberculous sputum, tubercles were macroscopically visible in the lungs, and the tracheobronchial nodes were distinctly enlarged. 2 The micro-organism may be carried by the blood stream, and, after passing through the walls of the vessel, may gain the lymphatic system and be conveyed to the tracheobronchial nodes. Krause<sup>7</sup> found that

After subcutaneous (right groin) infection of guinea-pigs with massive doses of tubercle bacilli they were found in the lung and tracheobronchial nodes at four days. At any given time during the period from four to twenty-six days after infection there are more bacilli in the tracheobronchial lymph nodes than in both lungs.

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5 Cunningham, R. S. On the Development of the Lymphatics in the Lungs of the Pig, *Anat. Record* **9** 69, 1915.

6 Rogers, J. B. Further Observations on the Artificial Tuberculous Infection of Guinea Pigs Through the Respiratory Route, *Am. Rev. Tuberc.* **3** 750, 1920.

7 Krause, A. K. Tuberculosis in the Guinea Pig After Subcutaneous Infection, with Particular Reference to the Tracheo-Bronchial Lymph Nodes, *Am. Rev. Tuberc.* **4** 135, 1920-1921.

the next meeting of the American Surgical Association in which I opened a tuberculous cavity and tried to make the resulting stoma permanent, it was impossible to do so, and the stoma closed. The patient still has tuberculosis.

Now as to the air embolism, if Dr. Graham will work with the patient's head lower than his heels, he probably will not get air embolisms.

DR. A. O. WILENSKY, New York. I have been much interested in Dr. Crowe's experimental work, because a number of years ago I tried to make an abscess of the lung, and the method I used was the following. I performed experiments on both dogs and cats. I took a bronchoscope and passed it into the trachea. As at that time there were many cases of abscess of the lung, there was no difficulty in getting the contents of the abscesses, and I injected the latter directly into the trachea. Either nothing happened or the dog was sick for a day or two and then gradually recovered, ultimately an abscess did not form. I think the dose of material was given so suddenly that the reflexes of the animal were sufficient to expel the mass of material injected. I am interested in Crowe's work for this reason, when a focus of suppuration is established in anatomic relation with the air passages, as by his method, the dose of infection is brought down constantly in small quantities, and I think that is the reason why the infection materializes into an abscess of the lung. It is interesting to note that so many of the children in whom Dr. Graham found sinus disease recovered after the condition of the sinuses was cleared up.

Among its several functions is the major one of limiting the spread of infections, and in no infection is this office so manifest and so well performed as in tuberculosis. Whether tubercle bacilli are inhaled or ingested, practically every natural infection begins at that moment when they shall have passed the mucosal epithelium and have gained the submucosa. There, between the cells of a bodily structure, they are always, first within the province of the lymphatic system, and all that are conveyed further will, within a microscopic distance be carried into lymphatic vessels and proceed by these for variable distances. At countless places they will meet with intercalated collections of lymphoid cells that range from the minutest aggregations to large lymph nodes. It is impossible to escape the idea that one of the resisting functions of allergy lies in the latter's ability to fix bacilli promptly where they settle and thus impede or prevent their further distribution. Lymphoid masses will act similarly, though in another way. In every instance in which infection is established we must believe that both the lymphatic system and allergy are contributing their part to the sum total of resistance.

When micro-organisms settle in a lymphoid mass or in a lymph node in the lung, they may (1) become destroyed in situ or remain latent, (2) inflammatory reaction may take place followed by healing, with or without deposits of calcareous matter, (3) suppuration may take place, and the node involved ulcerate into a bronchus, or (4) into the parenchyma of the lung and give rise to an abscess of the lung.

#### REPORT OF CASES

CASE 1.—A man, aged 33, had had measles and whooping cough in childhood, otherwise he had been well, although he had never been robust. Two months before he came to me for examination, he had noticed a slight pain a little above the right nipple and a slight cough accompanied by a scant but offensive expectoration of purulent material. The symptoms soon subsided. Twelve days later, he had a severe pain just above the right nipple, at the same time, he had an attack of coughing with the sudden expulsion of large quantities of extremely offensive smelling material. The patient had been working up to the time of the rupture of the abscess, which happened while he was being jolted in riding in an automobile over a railway crossing. He was then in bed for a while. According to his statement, he did not have fever throughout this sickness. The cough and expectoration gradually became less, and the odor disappeared. The lungs were normal, except for a few râles in the right lung. Results of the examinations of the sputum for tuberculosis were negative. Roentgenograms showed that the right lung had not cleared up in the triangular area (*a a a*, fig 3) that probably had been the seat of the abscess. The shadow, *b*, in the roentgenograms proved to be two concretions probably expelled from the cavity of the abscess into a bronchus. The patient was advised to have the concretions removed by bronchoscopy, but he coughed up the larger one without aid a few hours later. Bronchoscopy was postponed at his request. Two weeks later, he coughed up the smaller stone. The cough and expectoration gradually ceased, and the patient's health has been good. The suppuration probably started in the tissue surrounding the concretions in the bronchopulmonary nodes. Whether the micro-organisms had been latent or of recent arrival, they had apparently been of low virulence.

the trachea unaccounted for. The sum total of the contraction of all the muscles involved results in a sudden diminution of intrathoracic capacity, with a corresponding concentric rise in intrathoracic pressure. The latter is readily demonstrable with a pneumothorax manometer and needle inserted into the thorax during cough. And, furthermore, the height of the manometer reading during cough will be the same regardless of which portion of the chest cavity is tapped, thus demonstrating the existence of a uniform concentric rise in pressure from all sides. Hence, a uniform pressure is exerted on all portions of the lungs. An outlet for this increase in pressure is sought and is found in the sudden escape of air from the lungs through the trachea, larynx and buccal cavity. This sudden expulsion of air is recognized as the common manifestation of cough.

Any foreign substance in the tracheobronchial tree may be capable of stimulating the cough reflex. However, it has been demonstrated repeatedly that a tolerance to the excitation is rapidly obtained—in a matter of minutes—whereby the reflex is lessened and often temporarily entirely lost. On the other hand, all portions of the pulmonary tree are not equally excitable. Jackson<sup>2</sup> concluded from bronchoscopic observations that the finer subdivisions of the tracheobronchial tree, together with the alveoli, show decidedly less cough production from instrumental contact than the larger bronchi, while Reinberg,<sup>3</sup> working with the fluoroscope, found that secretions in the peripheral bronchial tree (filled through a bronchial fistula) did not produce cough in bronchi of the fifth, fourth or third order, cough being produced only when the second or first order or the trachea is filled. While operating under local anesthesia on a patient with a long standing pulmonary abscess which had recently been exposed by thoracotomy, we observed that cough was readily initiated when the larger communicating bronchi were probed. In a case of pulmonary abscess, opened through a large window in the chest, in the base of which there opened a number of bronchi and bronchioles, we made the observation that cough was readily initiated when a probe was inserted into one of the large bronchi, while a similar procedure was without effect in the case of the bronchioles.

Moreover, the act of coughing, although itself primarily a forced expiratory effort, is immediately preceded or followed by a markedly increased inspiration. This becomes most evident during a so-called spasm of coughing, when one observes a rapid succession of deep inspiratory and increased expiratory efforts.

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2 Jackson, C. Cough. Bronchoscopic Observations on the Cough Reflex, *J. A. M. A.* **79** 1399 (Oct. 21) 1922.

3 Reinberg, S. A. Roentgen-Ray Studies on the Physiology and Pathology of the Tracheo-Bronchial Tree, *Brit. J. Radiol.* **30** 451 (Dec.) 1925.



CASE 2—A man, aged 23, had had whooping cough at the age of 3 years. Shortly after this attack, he aspirated a brass cuff link. Since this accident he had had a cough, at first it was dry, but it gradually became purulent, and the sputum had a fetid odor. He had often had vomiting spells since the accident. The patient was referred to me at the age of 14. Roentgenograms revealed the cuff link in the right bronchus (fig 4). He had a right bronchiectasis and clubbing of the fingers. Bronchoscopic examination revealed a stricture of the right bronchus a little below the origin of the upper lobe bronchus. Granulation tissue and a great deal of pus were seen. The cuff link was removed. Some time later the patient returned, and he was advised to try bronchial lavage and treatment through the bronchoscope, but the advice was not accepted. At the age of 23, he again returned and wanted something done for the cough and for the foul expectoration. The sputum amounted to 300 cc in twenty-four hours,

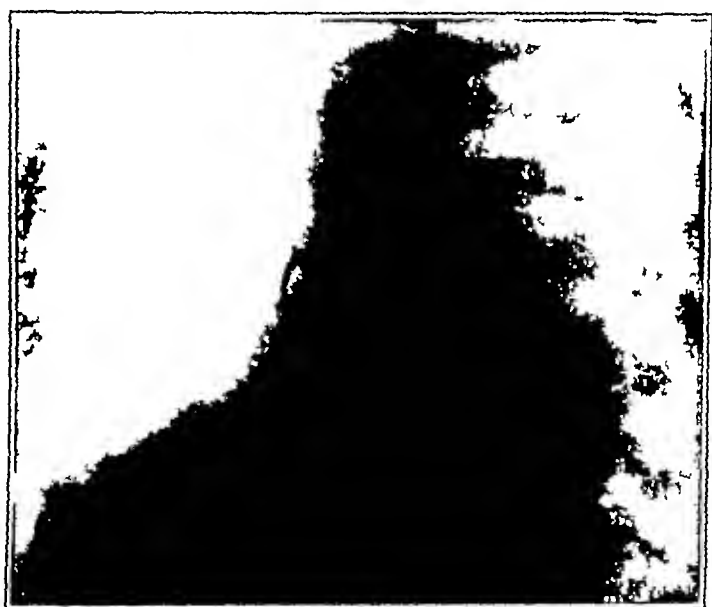


Fig 4 (case 2) —Roentgenogram showing the cuff-link in the right bronchus

examinations for tubercle bacilli were negative. The urine was normal. Roentgenograms after injection of iodized oil 40 per cent showed bronchiectasis of the middle and lower lobes of the right lung (fig 5). I intended to perform a graded thoracoplasty, but the patient developed cerebral symptoms and died of abscess of the brain.

Necropsy had to be limited to the right lung (fig 6). The lower and middle lobes were pink with darker areas of red. The upper lobe had the pigmented appearance usually found in the lungs of the adult city dweller. The right tracheobronchial groups of lymph nodes consisted of a firm reddish mass measuring 2.5 by 4.5 cm. The inferior group was similar in color and consistency and measured 2.5 by 5.5 cm. The groups of nodes at the angles of the division of the bronchi to the middle and to the lower lobes were large and firm, one measuring 3 by 1.75 cm. Nodes 2, 3 and 4 encroached on the vessels. The necks

16 Pancoast, H. K., Dunham, K., and Baetjer, F. H. Clinical and X Ray Findings in the Chest of Normal Children, *Am Rev Tuberc* 6:331, 1922

lobe of a tuberculous pulmonary cavity, and noted that the material dropped to the bottom of the cavity. With three successive coughs it was spread into the middle lobe, then transported to the lower lobe of the other side and finally coughed up. This important observation affords a visual demonstration of the spreading action of cough, and suggests the mechanism of the production of bronchial embolism. Ballon noted a similar phenomenon when iodized oil had been injected into the bronchiectatic cavities of a patient. After a few minutes cough was seen to empty the cavities and disseminate the oil widely throughout the pulmonary field. Ameuille points out that this illustrates how aspirated infectious material may be scattered by cough to all portions of the lung.

Still another mode may be suggested whereby, under certain conditions, the expiratory effort itself may be the means of spreading or forcing material deeper into the pulmonary tree rather than expelling it. For example, one may assume that there is a block, such as might be produced by a plug of mucus or a bronchiolar spasm, in a proximal bronchus. Then one may imagine that material distal to the block is forced toward it by the expiratory forces during cough, is unable to pass the block and then, immediately after cough, is carried on the rebound distally beyond its original depth of penetration either toward the original alveolus or now into new areas. Thus in figure 2 it is assumed that a block exists at *A*, then the material *B* approaches *A* during cough and immediately afterward is carried distally toward or into the alveolus *C*, or possibly into other alveoli distal to the block such as *D* or *E*.

However, regardless of the exact mechanism whereby the result is obtained, it has, as noted previously been repeatedly observed clinically that cough may be the means of spreading material in the tracheobronchial tree. The following experiments are presented with the view of demonstrating the truth of this assumption.

#### EXPERIMENTAL METHOD

In order to be able to visualize and secure permanent records of the action of cough on material in the tracheobronchial tree we used a substance which would cast a shadow by roentgen ray. The iodized oil was selected because of its excellent roentgenographic properties, the ease of its introduction, and the possibility of incorporating it with other substances. Three sets of experiments were planned: one with oil alone, another with equal parts of the oil and thick sputum (obtained from a patient with bronchiectasis) which were thoroughly mixed by being drawn back and forth repeatedly through a narrow mouthed syringe until a perfect emulsion was obtained of a fluidity approximately equal to the oil alone, and another with thick mucous mucus.

5 Ballon D. H. Lipiodol in the Diagnosis of Bronchopulmonary Lesions by the Bronchoscopic Method. *Arch. Otolaryng.* 3:405 (May) 1926.

of the bronchi to the middle and lower lobes were constricted, peribronchial fibrosis was marked at these points, and the bronchial walls were thick and fibrous. The nodes at the angle of division to the upper lobe were soft and anthracotic (fig 6). The difference in color between the upper lobe and the middle and lower lobes was striking. Microscopic examination of the nodes from the middle and lower lobes showed only a small amount of pigmentation, while the gross appearance of the nodes from the upper lobe was that of marked anthracosis.

Shingu<sup>17</sup> has shown that pigmentation is present in the lungs of human beings more than 23 days old. In the normal lung, some of the finer particles of carbon and other inhaled dust may enter the alveoli



Fig 7 (case 2)—Roentgenogram of the fresh specimen of the lung after injection with sodium bromide solution, and the various groups of nodes covered with lead foil corresponding exactly with their forms. The arrow points to the stricture caused by the cufflink. The right group of tracheobronchial nodes in the specimen was in close contact with the trachea and the right bronchus, with the lower pole overlapping the bronchus. The apparent separation is due to the angle at which the roentgenogram was accidentally taken.

and be carried by phagocytes through the alveolar wall to the lymphatics, which convey the dust-laden phagocytes to the tracheobronchial nodes. On their way thither, however, much of the dust is deposited in the tissues along the lymphatics, in the lymphoid masses and in the bronchopulmonary nodes. Pigments may be found in practically all the tissues

17 Shingu, S. Ueber die Staubinhalation bei Kindern. *Virchows Arch f path Anat* 200 207, 1910.

placed on an inclined plane of 30 degrees, head up, so as to facilitate the flow of the oil into the finer bronchi. Cats were the experimental subjects in all instances but one, in which a dog was used.

In nearly all of our own series of cases the injection was made by the bronchoscopic method. All the injections were made by Dr. David Ballou, of the department of otolaryngology in the Royal Victoria Hospital. We agree with his attitude that at least in the first injection of the oil the bronchoscopic method should be used, for the reason that this is the only method which can yield a satisfactory and direct visual examination of the injected field. Reference should be made to Dr. Ballou's papers for a full statement in this respect. Later injections may well be made by the indirect transglottic method, aided by proper posturing. The results of this method have been satisfactory when combined with the information afforded by the first bronchoscopic examination.

Preliminary experiments were then conducted in order to determine the rate at which iodized oil or the iodized oil-sputum emulsions flowed into the pulmonary tree under light general anesthesia. This was done by taking a series of roentgenograms at intervals of from two to three minutes, beginning immediately after injection. Four animals were used, two with the oil alone and two with the emulsion. The rate of flow in all instances was approximately the same. Thus, it was found that the larger bronchi were outlined in from two to four minutes, that from eight to ten minutes were required for good penetration of the finer bronchioles and that maximum penetration, as determined by the roentgen ray, took place in from twenty to twenty-five minutes. It is, of course, obvious that a true flowing action will not occur with masses of thick tenacious sputum, so that in experiments with this substance it was unnecessary to take into account the time element. Thus it was clear that if any "indrawing" action of cough were to be observed the cough should be induced as soon after the introduction of the material as possible and the roentgen ray record should be taken immediately. Therefore, the procedure was to introduce the material, stop anesthesia and take a control roentgenogram. By this time, about two minutes having passed, cough could be induced, following which another roentgenogram was taken all of which could be done in well under five minutes, and consequently before penetration of the finer bronchioles would normally have occurred. As soon as cough was obtained, narcosis was continued and this process could be repeated as often as desired so that one might watch the further action of subsequent coughs.

#### EXPERIMENTAL OBSERVATIONS

In the present article, we shall consider merely the direct action of cough on the material introduced into the tracheobronchial tree and shall purposely omit from discussion all secondary complications noted, such as pulmonary edema, pneumonia, massive collapse of the lung and the development of abscess of lung. We hope to publish these observations in the near future.

*Action of Cough on Iodized Oil or Iodized Oil-Sputum Emulsion.*—As similar results were obtained both with the oil alone and with the emulsion, they are considered under one head. Seventeen injections were made in this group two of which were unsuccessful because of

CASE 3—A girl, aged 19, had had measles at the age of 5. Since the attack she had had a cough and had expectorated a thick purulent material of a foul odor. The patient was well developed, the fingers and toes were clubbed. Examination of the chest revealed lagging in the base of the left lung, dullness in the left side below the fourth rib, bronchovesicular breathing on the left side below the second rib and in the right axilla, and moist, large râles over the left side of the chest on inspiration and especially on expiration. On bronchoscopic examination, purulent material was observed coming from both lungs and constriction of bronchial necks was noted. Roentgenograms showed heavy markings in both lungs, but especially at the divisions of the bronchi to the lobes on both sides, where pronounced fibrosis and calcified nodes were seen (fig 8). Points of calcification were seen toward the periphery of the lungs, probably indicating healed inflammatory processes in lymphoid masses. The diagnosis was bilateral bronchiectasis with abscesses following measles in childhood.

CASE 4—A girl, aged 24, complained of difficulty in breathing and a chronic cough with more or less purulent expectoration since she had had whooping cough at the age of 3, at the age of 21, she had had influenza. The amount of sputum varied, and at times it was relatively small, but she said that she had frequent "colds" with prompt increase of the purulent expectoration, there was no disagreeable odor to the expectorated material, and it was negative when examined for tubercle bacilli. She had a wheezy respiration and considerable dyspnea on exertion. The patient was of small stature, she had marked kyphosis and right scoliosis. The fingers were clubbed. The anterior wall of the chest was flat, expansion was limited, especially on the left side. Breath sounds came through better on the right than on the left side, the inspiration was more difficult on the left. There were many bubbling râles and squeals, especially on the left, pleural thickening on both sides, an area of dullness over the middorsal area and emphysema over the outer portions of the lungs. Roentgenograms showed fairly heavy markings throughout the lungs, particularly in the upper lobes, the bronchopulmonary nodes at the angle of division to the upper lobes and the tracheobronchial nodes were markedly enlarged, especially the left and inferior groups of the latter (fig 9). Bronchoscopic examination showed the trachea and left bronchus red and inflamed with an area of darker red to the left of the carina, purulent material was seen coming from both lungs. The diagnosis was bilateral bronchiectasis following whooping cough in childhood, with probable suppuration of nodes in the inferior tracheobronchial space. The attack of influenza three years previously may have given rise to the suppuration. I told the patient that the suppurative nodes might ulcerate through the tracheobronchial wall. A few weeks later, she wrote that she suddenly had coughed up pus that differed from the usual purulent sputum and that she felt better.

Bronchiectasis occurs in young children, and the majority of cases of bronchiectasis in adults that can be traced to childhood are sequelae to measles or whooping cough. Brauer<sup>20</sup> said

The statement that the majority of cases of bronchiectasis are congenital, is due to the fact that although in children inflammatory processes of the lung often occur as for example after measles, it is not always elicited in taking the history.

20 Brauer, L. Ueber Pathologie und Therapie der Bronchiektasien. *München med Wchnchr* 72: 964, 1925.



Figure 3

Fig 3 (cat 20)—Extent of penetration of iodized oil-sputum emulsion three minutes after injection without cough

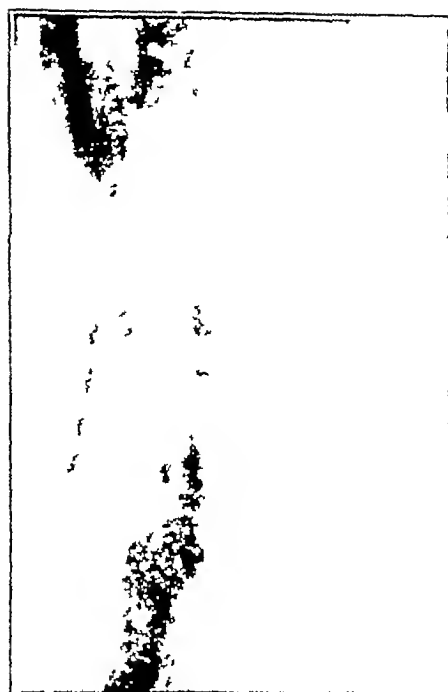


Figure 4

Fig 4 (cat 15)—Widespread penetration of iodized oil three minutes after injection and immediately after induced coughs without tracheal compression



Fig 5 (cat 11)—Fine diffuse spread of iodized oil particles three minutes after injection and one minute after induced coughs without tracheal compression

in four, and tuberculosis in one. In all these cases, enlargement of the bronchopulmonary and tracheobronchial nodes were found. The size of the bronchopulmonary nodes ranged between that of a pea to that of a small walnut, but in most instances, they were the size of a hazelnut or a kidney bean. The tracheobronchial nodes varied in size from that of a pea to that of a small hen's egg. Thirteen of the twenty cases were complicated by bronchopneumonia, which accompanied whooping cough in nine of the cases. The average time from onset to death in the ten cases of whooping cough was about twenty-eight days.

In the majority of cases of infection of the bronchi or of the lungs, the micro-organism enters the lower respiratory tract by inhalation. After penetrating the epithelial lining, it reaches the submucosa and at once enters the lymphatics and begins its journey toward the tracheobronchial nodes, which it may reach unless intercepted by one of the interpolated lymphoid masses or nodes. With continued microbic invasion, the nodes enlarge and may ultimately become blocked, and as the lymphatic drainage fails, the micro-organism wanders through the lymphatic wall into the surrounding tissues, where inflammation ensues. The inflammatory process may subside and healing take place, or it may progress and become chronic, the enlarged nodes (by pressure) and the inflammation in the bronchial wall or in the peribronchial tissue thus furnishing two factors inductive to the development of bronchiectasis. As the inflammatory process spreads, it involves the musculature, the elastic tissue and the cartilages of the bronchial walls, and the surrounding tissues. With infective material stagnating in the obstructed bronchi, the pathologic picture of destruction in advanced bronchiectasis described in textbooks gradually develops. The rapidity with which lymph nodes increase in size is notable in one of the cases reported by Forgeron,<sup>1</sup> that of an infant, aged 3 months, who died a few days after the onset of influenza. At necropsy, congestion of the lower lobes with edema was found. Bronchopulmonary nodes formed masses the size of large hazelnuts, associated with periadenitis, the tracheobronchial nodes were seen in masses varying in size from that of a small kidney bean to that of a large almond. It seems probable that the congestion and the edema of the lower lobes in this case may have been caused by pressure on the vessels by the swollen bronchopulmonary nodes.

In case 4 in a paper recently published by me,<sup>2</sup> enlarged tuberculous eparterial nodes compressed the bronchus to the complete obliteration of its lumen, in case 3 in the same paper, the enlarged left tracheobronchial nodes (nontuberculous) caused pressure on the left main bronchus. In case 2 in the present article, the bronchopulmonary nodes at the angle of division of the middle and lower lobe bronchi caused pressure on the vessels, and the bronchial necks were fibrous and strictured. In

*Action of Cough on Tenacious Sputum Injected with Iodized Oil*—Six injections were made, all through a tracheotomy tube. The first two attempts were unsuccessful, as the injected material blocked the trachea and the animals died of asphyxiation. It was then found that if the mass was injected at the beginning of an inspiratory effort it would be carried to a point just beyond the bifurcation, and hence at least unilateral respiration might continue. Thus, in four instances we were able to note the effect of induced cough plus tracheal compression on thick tenacious sputum. It was observed that although the mass might be forced slightly into the larger bronchi it was not broken up nor forced into the finer bronchioles or alveoli. Thus, the material came to rest in a sensitive area in which it might subsequently induce normal reflex cough. This was found to take place, and subsequent roentgenograms showed that the material was soon expelled. Figure 9 shows the masses fairly intact, and in figure 10, taken after cough with tracheal compression, no great change is noted, while in figure 11, taken thirty minutes later, no foreign shadow is noted, the material having been expelled. Apparently, then, whereas cough may tend to drive a fluid substance such as iodized oil or iodized oil-sputum emulsion deeper into the pulmonary tree it is incapable of similar action on such material as thick tenacious sputum.

#### CLINICAL APPLICATION OF THE OBSERVATIONS

Since it has thus been shown that cough may actually force material similar in consistency to iodized oil deeper into the pulmonary tree, the question logically follows whether or not, in certain surgical procedures cough is not more likely to be a danger than to produce safety. If this were the case, the aim should be to abolish rather than to maintain the cough reflex. This problem arises particularly in thoracoplastic operations for the compression of a tuberculous lung containing cavities. A considerable quantity of fluid pus may suddenly be expressed into the trachea and larger bronchi as a result of operative manipulations and falling in of the chest wall. In patients operated on under local anesthesia as so generally recommended (in order to preserve the cough reflex), or under extremely light general anesthesia cough would be induced immediately. It is likely then, that the patient while getting rid of a part of the pus, might easily force some of it into the alveolar spaces of the healthy lung. Having arrived in the alveoli it may readily remain a sufficient time to cause by contact an acute tuberculosis. On the other hand, this complication might be obviated by the use of general anesthesia and by sufficient morphine both before operation and for at least twenty-four hours thereafter to abolish the cough reflex and the possible effect of gravity can be obviated by operating on the



Macklin<sup>24</sup> has described the elastic membrane and the part that he thinks it plays in the "recoil mechanism" of the bronchial tree. It seems to me that if the nerves to the affected lobe should become involved by pressure or infection, the physiologic movements of the bronchi in that area might be curtailed or abolished, and that a more or less complete relaxation of the bronchial walls would take place, thus changing the bronchi into passive and fixed receptacles for the accumulating purulent material.

CASE 5—A child, aged 12 months, according to the mother, had been in good health until it suddenly became sick with a severe cold three weeks before entering the hospital. The attending physician had made a diagnosis of bronchitis.

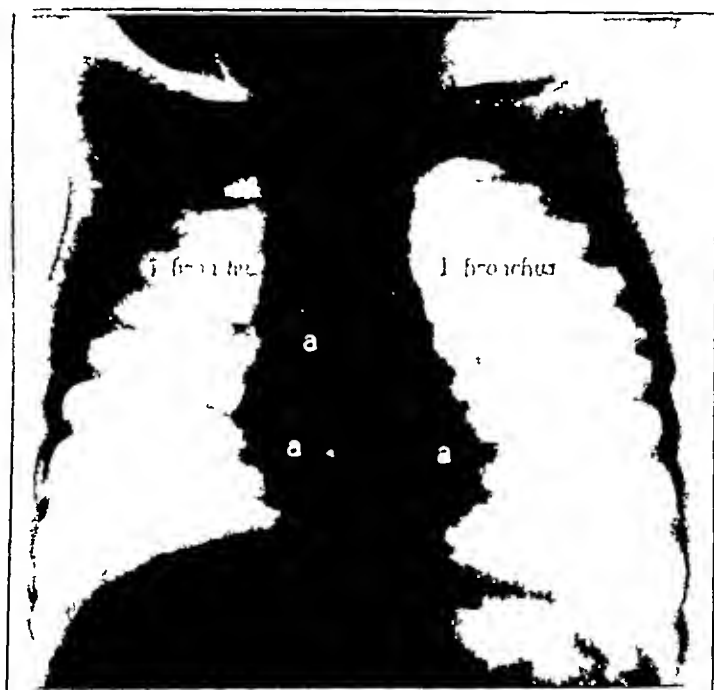


Fig. 10 (case 5)—Roentgenogram showing collapse of the right lung, particularly the upper lobe, right main bronchus at almost right angle, abscessed nodes (*a, a, a*) in inferior tracheobronchial space.

There had been increasing difficulty in respiration, and inhalations of steam had been used. The mother said that the child had not had fever. There had been a brassy cough. During the third week of sickness, there had been a gradually increasing dysphagia. It had been suspected that there was a foreign body in a bronchus, and the case was referred to me. On the night of admission, the child's temperature was 100 F by rectum, the pulse rate was 110, respiration, 30. Dyspnea was marked, and a steam tent was used. Except for the finding of moist râles over both lungs, the results of the physical examination were negative.

24 Macklin, C. C. A Note on the Elastic Membrane of the Bronchial Tree of Mammals, with an Interpretation of Its Functional Significance, *Anat. Record* 24: 119, 1922.

## SUMMARY AND CONCLUSIONS

- 1 The physiology of the act of coughing is considered
- 2 The experimental results of the action of cough on iodized oil, iodized oil-sputum emulsion and thick, tenacious sputum which had been injected intratracheally into cats, are presented
- 3 It was observed that cough alone increased the rapidity and degree of penetration of iodized oil and iodized oil-sputum emulsion, this was even more marked when tracheal compression was applied thus showing an actual "indriving" action of cough



Fig 11 (cat 13) —Taken after the removal of the tracheotomy tube, cessation of anesthesia and thirty minutes after figure 10. No foreign shadow is shown, the material having been expelled.

- 4 A similar "indriving" action of cough on thick tenacious sputum was not noted
- 5 The relation of cough to certain postoperative pulmonary complications is briefly discussed
- 6 It is concluded that cough may tend to drive fluid substances similar to iodized oil deeper into the pulmonary tree and that it is incapable of like action on a heavier substance, such as thick tenacious sputum
- 7 We wish especially to draw attention to the fact that the ordinary usual action of cough is to expel material from the tracheobronchial tree, it may under certain conditions, actually bring about the opposite result that is drive material deeper

measuring 2.5 by 2 cm. The nodes in the inferior tracheobronchial space formed a mass 3.5 by 3 cm., containing from about 3 to 4 cc. of pus. The mass was adherent to the esophagus, to the pericardium, to the bifurcation and to both main bronchi, as well as to the adjacent part of the right lung, which showed a limited consolidation in the corresponding area. The mass extended to the spinal column, displacing the esophagus posteriorly and to the left (fig. 11). Where the mass was in contact with the pericardium, the esophagus and the bifurcation, the lymph node tissue had ulcerated away, so that the wall of the abscess at these three points was formed by the three structures named, the abscess, therefore, might have ulcerated into any one of the three organs. Results of examination for tubercle bacilli and other micro-organisms in the pus were negative. Injections were made into a guinea-pig, unfortunately, it died in eighteen days. Microscopic sections showed caseous tuberculous lymph nodes. The cultures taken through the bronchoscope showed *Streptococcus viridans* and *Staphylococcus aureus*.

The previous good health of the child, a sickness of only three weeks' duration, with gradually increasing dyspnea and dysphagia, should have made possible a diagnosis of formation of an abscess.

Any major operation in so young a child with pronounced difficulty in breathing would obviously have been out of the question. The only chance for recovery would therefore have been through a spontaneous rupture into the bronchial tree. In the literature there are reports of necropsies on children who died following ulceration of abscessed tuberculous nodes into the bronchi, in these cases, scars were found elsewhere in the bronchial walls, indicating that similar processes had taken place before and had been followed by complete healing. In a recent paper,<sup>2</sup> I reported cases in which large nontuberculous abscesses of the tracheobronchial nodes ulcerated into the bronchi, followed by prompt recovery. The rapidity with which these abscess cavities closed was astonishing. In one of the cases, I observed the opening in the tracheobronchial wall through the bronchoscope on the third day after the discharge of the abscess, and it was remarkably small. As it is impossible to foretell whether an abscess in one of the tracheobronchial spaces will ulcerate into the bronchial tree or into one of the surrounding organs, it occurred to me that "puncture" of the abscess through the tracheobronchial wall would be a logical procedure in cases seen in the advanced stage and in which death was imminent from obstruction to respiration. To this end I have devised an instrument to be operated through the bronchoscope, as shown in figure 12. The bronchoscope devised by me has four channels, namely, one for the light carrier, one for the operating instrument, one for suction and a larger one through which the surgeon can observe the field of operation unhampered by the instruments introduced. The operation should be performed under the guidance of the eye, therefore the shank that carries the knife blade is flexible proximal to the blade, so that the latter can be brought into view by pulling the wire (fig. b). The shank runs



0.3 cm in a child 1 year old and from 0.3 to 0.5 cm in adults would probably reach the abscess cavity. The visualization of the topographic anatomy in the area to be punctured is imperative. On the proximal part of the shank is a guard with a set screw and a millimeter scale, so that the surgeon can limit the depth of the puncture by setting the guard. The wall of the abscess may be unevenly thick, and the first puncture may not reach the pus cavity, it therefore may have to be repeated a little distance away. The instrument for "puncturing" is placed in the bronchoscopic channel before the latter is introduced into the trachea, and the operation can be quickly performed, it should be done with the patient in the Trendelenburg position and under local anesthesia in adults and without anesthesia in children.

This method of operating first occurred to me four years ago after bronchoscopic examination in case 4, but I did not have the instrument for "puncturing" made until after the necropsy examination in case 5. In this case, the method described would be the operation of necessity, in cases 1 and 2 in my recent paper,<sup>2</sup> it would be the operation of choice.

#### SUMMARY

The lymphatic system is the drainage apparatus of the lung. Inhaled dusts, after entering the pulmonary lymphatics are carried in the lymph current toward the central depot, i. e., the tracheobronchial nodes, and so are bacteria whether inhaled or blood-borne. On their journey toward the tracheobronchial nodes, bacteria may be intercepted and settle in lymphoid masses or bronchopulmonary nodes.

Much attention has been paid to tuberculous infection of the tracheobronchial nodes, while nontuberculous infections of these nodes have received little notice. Tuberculous as well as nontuberculous infections of the tracheobronchial nodes occurs in both children and adults. The bronchopulmonary nodes have received little attention clinically yet they may be the source of abscesses of the lung. Tuberculous as well as nontuberculous suppuration occur in these nodes. The tracheobronchial and particularly the bronchopulmonary lymph nodes may be potent factors in the causation of bronchiectasis in childhood.

I have not found any clinical reference to the lymphoid masses, but as they, like the lymph nodes, act as filters, bacteria may settle in them, and they may therefore become centers of suppuration.

The healing of inflammatory processes in the lymph nodes is often followed by calcification. Such concretions in the tracheobronchial and the bronchopulmonary nodes not infrequently ulcerate through the bronchial wall and are expelled by mouth. Concretions in the bronchopulmonary nodes may ulcerate into the parenchyma and give rise to abscess of the lung. In roentgenograms of the chest, points of

for cough which is, to be regarded as of advantage to the patient when it leads to the expectoration of abnormal material in the air passages such as foreign bodies, blood and secretion. From one tenth to one third of the inhaled foreign bodies are thus expelled. When there is profuse bleeding into the air passages or flooding with abundant pus from the rupture of abscess or empyema, death from asphyxia is likely unless the fluid can be expelled. If, under such circumstances, the expulsive power of cough is impaired by artificial pneumothorax, or the cough reflex is absent in consequence of unconsciousness from anesthesia or other cause, the danger is much increased.

On the other hand, under certain circumstances cough may be a source of considerable danger. With a weak myocardium, cough caused by an acute respiratory infection or passive congestion may overtax an already burdened heart and become an important contributing cause of cardiac failure. With hemoptysis caused by tuberculosis, cough may dislodge the thrombus in a bleeding vessel and lead to renewed hemorrhage. In the presence of pulmonary tuberculosis, the exertion and heightened air pressure within the thorax caused by cough may activate or keep active the tuberculous process. The expulsion by cough of infected material from one place to another in the bronchial tree may spread infection into previously uninvolved regions.

Considering these good and ill effects, it is no wonder that there is little unanimity of opinion as to the treatment of cough. On the whole however cough, in spite of its dangers, is usually to be regarded as of advantage to the patient, and should ordinarily be treated only by those methods which attempt to improve or eliminate the cause. It would certainly seem safer not to attempt to subdue cough and expectoration by drugs when there is such foreign material within the air passages as blood or pus. But when the patient is harassed and fatigued, and his sleep is disturbed by unproductive cough, it may then be desirable to attempt its control by drugs even though some risk may be taken by so doing. If I understand Dr Archibald's experiments correctly, there is nothing in his results which indicates that it would be desirable to change this practice, as material of the consistency of tenacious sputum did not appear to be driven further into the lung by cough.

DR J. M. BISAILLON, Portland, Ore. The work which Dr Larrell did at the University of Oregon in demonstrating sensory nerve filaments in the lung might have an important bearing on this subject particularly as to the nature of the cough reflexes which are under discussion. The sensory nerve endings were found more in preponderance at the height of the tree at the point of division of the bronchi.

DR F. A. C. SCRIMGER, Montreal, Que. One or two points occurred to me in respect to Dr Graham's reference to the activation of tuberculous infection by use of iodized oil, it is a real danger and I have encountered it several times.

Smaller bronchi are less irritable than larger bronchi. I recall a case in which Dr Archibald directly opened an abscess cavity and the cavity walls entirely free from any cough reflex. Smaller bronchi could be touched or probed readily without producing cough while probing of the larger bronchi immediately results in cough.

Regarding postural drainage, I recall a case of tuberculosis with cavitation. During the progress of the disease 10 to 12 ounces (0.4 to 0.52 Gm.) of fluid pus ran out of the chest after drainage effort on the part of the patient. The fluid was very thick and sticky and rested on the rest of the body. After operation there was no further drainage of pus or infection. The degree of fluidity of the pus was such that it could be

One type progresses to straight formation of a mediastinal abscess and is not relieved except by mediastinotomy. The second type breaks into the bronchus and drains in that way. The third type apparently subsides without the formation of an abscess.

Dr Lerche's observations and his instrument for dealing with the type of infection that does not break through the trachea and is difficult of access is exceedingly interesting.

Dr N. W. GREEN, New York. Time does not allow for a long discussion of Dr Lerche's cases. I have done some intratracheal and intra-esophageal work for the past nineteen years, and I have used Dr Lerche's instruments. I have always been impressed with the ingenuity with which they were devised. I think Dr Lerche has courage and skill and vision in his work.

Dr MARTIN GRAHAM, St. Louis. I want to say just a word or two, particularly about the suggestion Dr Lerche makes concerning the relationship of enlarged tracheobronchial glands to the production of bronchiectasis. The work of Mullin of Cleveland has been constructed largely around this idea. I felt that from previous remarks most of the members of the society were not familiar with it. It is interesting work—the work of a rhinologist who has produced enlargement of the tracheobronchial glands experimentally in animals by infection of the nasal sinuses. It closely simulates the work that Dr Crow has already reported, although Dr Mullin did not produce abscesses of the lung, but produced enormous enlargement of the tracheal glands. He has made the interesting suggestion in several of his articles that bronchiectasis in children may be due to the pressure effects of enlarged tracheobronchial glands resulting from infection of the nasal sinuses.

As I said in a previous discussion, I have felt that there is more than a grain of truth in this idea, and it is for that reason that for some years we have been paying almost as much attention to the nasal sinuses in chronic pulmonary suppurations as we have to the lungs. It has been gratifying, even in chronic cases, to see the pulmonary symptoms clear up after proper attention to the nasal sinuses. One sees this sort of thing happen repeatedly. In a child with the history of many years of chronic pulmonary suppuration, even with moderate or advanced bronchiectasis, with extensive suppuration in the nasal sinuses, the suppuration in the nasal sinuses cleared up and the child stopped coughing. He may go along for eight months or a year without any evidence of pulmonary involvement except the coughing up of a little sputum in the morning, but he is practically free from all of his former symptoms. He has an attack of acute coryza, the nasal sinuses are acutely infected again, and he is brought back with all of his former symptoms—cough, sputum and fever. After he has been kept home from school for a couple of weeks, and fairly conservative treatment administered, by means of repeated washing out of the nasal sinuses, the pulmonary symptoms again promptly disappear. Sometimes, if one is persistent and patient enough after two or three cycles of the first event, the child will not have any further attacks of pulmonary suppuration. I am sure, therefore, that there is some connection between enlargement of the tracheobronchial glands and chronicity of pulmonary suppuration. Whether or not it is from pressure, I am not prepared to say.

One other point Dr Lerche brought up is the question of the discharge from the tracheobronchial glands into the trachea of calcified bodies, so-called broncholiths. Broncholiths are not uncommon. In my own experience, I have found them present in 2 per cent of all cases of bronchopulmonary suppuration. One has to be careful in trying to find them because they are small but until all the

bronchi or bronchiole divide (fig 2) In regard to the masses of lymphoid tissue, Miller<sup>4</sup> said

They should be of interest to the pathologist as well as the clinician for these masses frequently serve as centers to which by means of the lymph vessels disease processes may be conveyed The smaller masses of lymphoid tissue may like the lymph nodes, act as filters interpolated in the lymph circulation They also serve as centers to which phagocytes carry their collected material I have followed through serial sections numerous small tubercles situated in the parenchyma of the lung, in every instance I have been able to trace their origin to one of the situations in which I have described lymphoid tissue as being present in normal lung

The lymphatics of the lung are found in the walls of the bronchi along the arteries and veins and in the pleura In the bronchi that

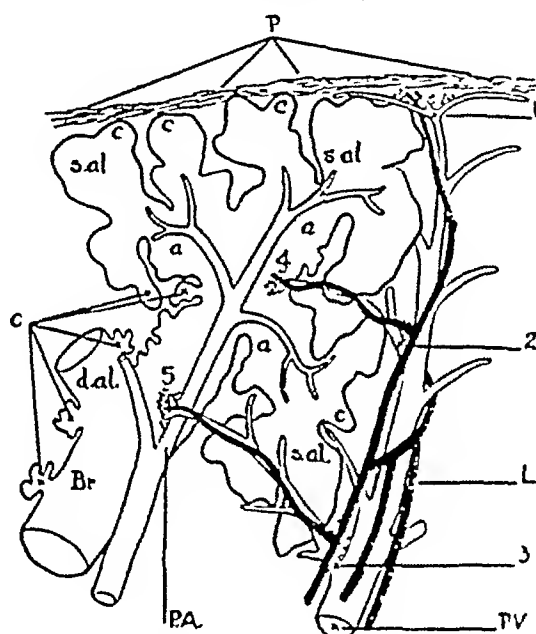


Fig 2—Schematic longitudinal section of a primary lobe of the lung showing bronchus, pulmonary artery, pulmonary vein, and lymphatic vessels. 1, 2, 3, 4, 5 the five points mentioned in the text. The lymphoid tissue is represented by the stippled area. P, pleura (Miller)

possess cartilages two sets of lymphatics are arranged to enclose the cartilages and are connected with each other by vessels between the cartilages There is a single plexus of lymphatics in the smaller bronchi Lymphatics do not occur in the alveoli The normal flow of the lymph in the lung is toward the hilum part of the pleura is toward the hilum There is a plexus of lymphatics in the pleura these lymphatics are connected with the

<sup>4</sup> Miller, W. S. The Distribution of Lymphatics in the Lung. Anat. Record 5: 99, 1911



# THORACIC SURGERY IN AMERICA

A RETROSPECT AND AN OUTLOOK

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NEW YORK

On looking back over the last thirty years, one sees that it was principally Fell of Buffalo, Matas and Parham of New Orleans, Green and Janeway of New York, Quenu and Tuffier of Paris, and Garré, Kuttner, Friedrich and Sauerbruch of Germany, the latter then assistant at von Mikulicz's surgical clinic in Breslau, who in their combined though independent pioneer work laid the foundation for the structure soon to be erected, and gave the principal impetus to the evolution of thoracic surgery in its present modern garb.

True enough, even before that, the chest had frequently been incised with impunity without the help of apparatus designed for the avoidance of the acute pneumothorax. The surgeon had simply taken a chance, because methods for the definite exclusion of such an occurrence, with its possible fatal result, were not known at that time. The opening, with perfect safety and pursuant to a definite plan, of the so-called "angin" pleural cavity—that is, one without adhesions between the visceral and the costal pleura and without the after effects of a former acute subacute or chronic inflammation—and the method of operating within the thorax with the same safety, equanimity of mind and results as in the abdomen date from the work of the men just mentioned. All of this work was performed in the last years of the nineteenth and in the beginning of the twentieth century. The time from 1898 to 1904, therefore, should be considered as that of the birth of modern thoracic surgery.

At that time only a spark was needed to set aflame this material gathered from the various countries in order to illuminate the whole civilized world. This spark was supplied when the American Medical Association, through its Section on Surgery and Anatomy, placed on the program of the annual meeting to be held in Chicago in 1908 an international symposium on "Intrathoracic Surgery." Professor Schaefer of London and Dr. Sauerbruch, then professor extraordinarius of the University of Marburg, were the invited guests, together with representatives of the American medical profession, foremost among whom were Samuel Robinson, Nathan W. Green, H. H. Janeway, George E. Fell and John B. Murphy, men particularly interested in this chapter of surgery. The year 1908 might therefore be considered the beginning of modern thoracic surgery on a larger scale in America.



in Washington, in 1922, that, for the sake of safety, apparatus for the use of differential pressure should always be on hand when the thorax was to be entered. In other words, the surgeon who incises the chest without such preparation takes unjustifiable chances in handling the patient, whose life it is his duty to protect with all available means.

Meanwhile Gwathmey, following Tiegel's principles, adapted his well known anesthesia apparatus to the needs of thoracic surgery by fastening the rebreathing bag, which had already been in use for many years, tightly on the face of the patient. The application of the usual mixtures of various anesthetic gases plus oxygen under pressure, wherever employed with the help of this apparatus, was found to be sufficient, simple and safe. Some surgeons still made use of pharyngeal anesthesia by blowing the gas under pressure directly into the pharynx through tubes placed in the nostrils. The negative chamber, positive pressure cabinets and intratracheal insufflation had become obsolete.

At the Lenox Hill Hospital in New York, the space occupied by the thoracic pavilion was given to the roentgen-ray department, which could not find any other quarters and which needed to expand. This necessitated the dismantling of the negative chamber in 1923, of course, all parts were saved and stored. But will the chamber ever be reconstructed? Most likely not. From a purely scientific standpoint, the dismantling of this negative chamber must be considered a loss, for it was the most complete physical apparatus of its kind in the world. It might have been useful in the future in emergencies, e. g., in acute emphysema of the mediastinum and the extrathoracic soft tissues and also in complicated postoperative conditions. In such instances it might save life when all the usual hypodermic, intravenous and chemotherapeutic attempts, including blood transfusion, have failed and only such physical means, the breathing of oxygenated air under pressure *for a number of hours*, can restore proper heart action. Patients not completely enervated may perhaps stand the rubber rebreathing bag over the face for hours without being anesthetized, but I am sure that the majority will be too feeble and will eventually die. I believe that a cabinet of some kind is required in such cases, so that the patient will be in an almost sitting posture, with the apparatus covering the head—somewhat on the lines of the old Brauer apparatus. In such a cabinet the patient will be able to breathe air and oxygen under pressure with comfort for as many hours as may be found necessary to overcome the great danger of a failing and otherwise intractable heart muscle.

I shall never forget an experience I had in 1910. After a bilateral vagolysis for a sacculated esophagus consecutive to cardiospasm of long standing performed on a depleted woman, aged 46, the heart failed to respond to the usual means of stimulation. The placing of her head for nine hours in our plus-pressure cabinet, the only one available at that



hospitals, they will find up-to-date help, and the lives of many will be saved by careful, trained observation and by timely intervention. But what facilities do they find in smaller communities with the less elaborate, but always well equipped, hospital? In many places such patients are often left to die after a diagnosis of severe "internal injury," because the teachings of present day thoracic surgery have not yet reached the medical profession at large. Those who are now called on to minister to this class of patients with severe internal injury of the chest have not received the training in this branch of medicine at the medical colleges that they have received in performing operations on all other parts of the body.

The teaching of thoracic surgery, at least of its principles, is therefore a much needed addition to the medical curriculum. Probably some have already introduced it, or are about to do so, but as far as I know, this has not been done in medical colleges at large, and yet this training is an absolute necessity. It will, of course, burden still more the already overcrowded curriculum of the medical students, but wise adjustment by the proper committees will overcome this difficulty. Less important subjects may be left out and thoracic surgery added. At present, the student is required to know the anatomy and physiology, perhaps also in some colleges the surgical pathology, of the chest and the organs it contains. Operative surgery of the chest, radical and conservative, and after-treatment should be added. It is so fascinating that, once begun, the majority of students will be enthusiastic over it, and the young surgeons I feel confident, will never give it up, they will be glad to add it to their daily routine. They will quickly realize the necessity of being prepared to meet the possible dangers of acute pneumothorax, and that the technique of operations within the chest is not different from that of operations on the abdomen, they will also see that it is not proper for the well trained surgeon to draw the dividing line of his work at the diaphragm, thus being obliged to leave surgical conditions above this muscle to someone specially trained.

While it is proper for large institutions with many hundreds of beds and with a vast amount of material to have specialists for every branch of surgery, scientific and operative, this cannot be done in small towns. If not all, at least the majority, of the members of the attending staff of smaller hospitals will soon have to take active interest in the cure and alleviation of patients with thoracic diseases. From the attending physician down to the adjunct, they will have to meet on common ground, they will have to cooperate and establish the borderline in sub-acute and chronic cases when the patient's treatment must pass from the internist or specialist to the surgeon. And what a benefit this will mean for the further rapid, more detailed evolution of this branch of surgery. Many minds working in the same direction usually obtain better, quicker and more important results than does one man working alone.



Fig 5 (case 2) —Roentgenogram showing bronchiectasis of the right middle and the lower lobes, after injection with iodized oil 40 per cent. The arrow points to the stricture caused by the cufflink.

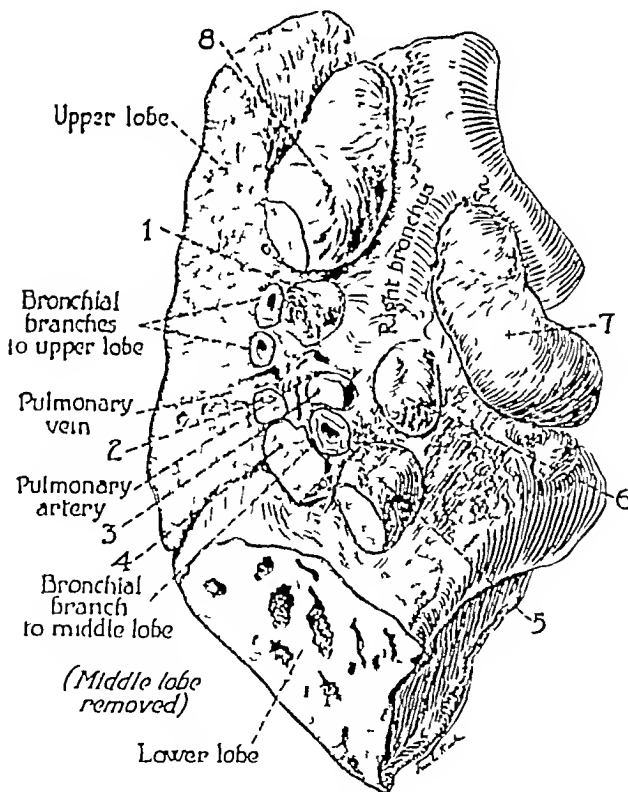


Fig 6 (case 2) —Drawing showing hardened specimen of the lung. 1 to 6 indicates bronchopulmonary nodes, 7, inferior tracheobronchial nodes, 8, right tracheobronchial nodes, 2, 3 and 4 are encroaching on the vessels, 4 is encroaching on the middle lobe bronchus.

# SUPPURATIVE PERICARDITIS

REPORT OF THREE CASES \*

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Suppurative pericarditis is a disease not often recognized during life, which accounts for the relative rarity of the performance of pericardiotomy. Only slightly over 100 operations for the relief of this disease are recorded in the surgical literature. I have added the reports of three cases.

## CASE REPORTS

**CASE 1—History**—Joseph Giordano, aged 1 year, of Italian parentage, was admitted to the babies' ward of the New York Post-Graduate Hospital on Nov. 14, 1916. He was breast fed and previous to the present illness had been healthy. For four weeks before admission to the hospital, he had been ill with fever, rapid breathing, cough and an expiratory grunt. After two weeks there was improvement for a few days, followed by a recurrence of the symptoms. The appetite was fair; the infant did not vomit and slept poorly. On admission, he weighed  $21\frac{1}{4}$  pounds (9.6 Kg.), the temperature was 99.2 F., pulse rate, 140, respiration, 52. The infant was fairly well nourished and developed. He appeared acutely ill and was dyspneic.

**Physical Examination**—The head and the neck presented nothing abnormal. The lips were dry and scabby, the tongue was coated and the buccal mucosa was clean. The child had four upper and two lower teeth. The pharynx and heart were normal. Many mucous râles were heard over both lungs, there was dulness over the left lower lobe, posteriorly. Bronchial breathing was not heard. The abdomen was moderately distended and tympanitic. No masses were palpable, and there was no point of tenderness. The liver was palpable 2 cm. below the costal arch. The spleen was not felt. The extremities were normal except for some swelling of the dorsa of the feet.

A provisional diagnosis of resolving pneumonia was made.

**November 16** A roentgenogram of the chest showed consolidation of the lower lobe of the left lung.

**November 18** Scattered subcrepitant rales were heard throughout both lungs, posteriorly. Over an area of the chest, anteriorly, from 2 cm. to the right of the sternum to the left midaxillary line, respiratory murmur and cardiac sounds were distant. Bronchial breathing was heard at the apex of the left lung.

**November 20** A roentgenographic examination showed a fairly extensive pericardial effusion. Pleural effusion was not present.

**November 23** Dr. Roger Dennett aspirated about 25 cc. of thick greenish-yellow pus from the pericardium. A culture showed *Bacillus influenzae*.

**Operation**—On November 25, with the infant in a semisitting posture, a local anesthesia (0.5 per cent procaine hydrochloride solution) was given and a curved incision made along the left margin of the sternum and out over the fifth costal cartilage. The cartilage was resected, the internal mammary artery

of the lung. Miller<sup>18</sup> stated that the quantity of lymphoid tissue in the lung increases from childhood to old age owing to irritation from the continuous deposits of dusts. In case 2 the patient had just had whooping cough which is always accompanied by some bronchial infection and probably also infection of the bronchopulmonary nodes when he aspirated the cuff link. Fresh infection was thereby superimposed, and the already infected nodes became blocked with infective material, which extending from the lymphatics into the surrounding tissues gave rise to inflammation and destruction of the lymphatics. Hence dust was



FIG. 8 (case 3).—Roentgenogram showing marked fibrosis and calcified nodes at the division of stem bronchi on both sides especially in the right lung at *a* and *b*. Abscess at *c*. Bilateral bronchiectasis and abscess. The left side was injected with iodine oil 40 per cent.

not carried to the middle and lower lobes. Coffin<sup>18</sup> found that lymphatics will grow into granulation tissue but where there is a chronic inflammatory process with new infection constantly added the lymphatics are destroyed as shown by Koester<sup>19</sup>.

18 Coffin T. H. On the Growth of Lymphatics in Granulation Tissue. *Bull. Johns Hopkins Hosp.* 17:277, 1906.

19 Koester. Die Bedeutung der Lymphgefäße bei der chronisch-granulierenden Entzündung. *Berl. klin. Wchnschr.* 20:748, 1883.



The heart beat was rapid but regular. Murmurs, enlargement or displacement were not noted. The abdomen was flat and tender, masses, rigidity or hernia were not present. The liver and spleen were not palpated. The extremities were normal. The knee jerks were equal but sluggish, otherwise the reflexes were normal.

The temperature was 101 F, respirations, 36, pulse rate, 132.

The following morning, on examination of the chest, a few small, crackling râles were heard just outside and below the left nipple. Bronchial breathing was heard over the same area. Dulness was not noted on percussion over this area. Urinalyses were negative. The diagnosis of bronchopneumonia was made.

A complete blood count revealed hemoglobin, 70 per cent, red blood cells, 4,600,000, white blood cells, 13,200, differential count polymorphonuclears, 68 per cent, lymphocytes, 31 per cent, eosinophils, 1 per cent.

*Course of Illness and Operation*—The child apparently improved rapidly after admission, and on the third day of her stay in the hospital the temperature became normal, respirations were about 28 and her pulse rate, 120. On the fifth day, after her temperature had been normal for two days, she had a sudden rise in temperature to 104 F, the pulse rate became more rapid (144) and respirations rose to 60. Examination of the chest at that time apparently did not show any abnormality of the lungs. Examination of the heart showed a slight enlargement of the cardiac area to the left, but none to the right of the sternum. No friction rub or murmurs were heard. The heart sounds were somewhat distant and weak. The roentgen-ray examination revealed the total area of the heart markedly increased and the borders of the heart straightened with a broadening in the region of the superior vessels suggesting the likelihood of pericardial exudate. Another roentgen-ray examination was made the following day and the foregoing symptoms were confirmed.

The symptoms remained about the same, and on June 23, eight days after admission to the hospital, the pericardium was aspirated and a small amount of thick yellow pus was obtained. The needle was inserted in the fifth intercostal space about 0.5 cm to the left of the sternum and was pointed upward and toward the right side.

There is much discussion as to the best site for a pericardiocentesis. Osler says that the fourth or fifth intercostal spaces near the sternum are the sites most often selected. Hibblom advises the fifth interspace just inside the left border of dulness. Kocker recommends the fourth or fifth interspace to the right of the sternum, if there is considerable dulness to the right. If the diaphragm is depressed, Osler says that the best point is high in the angle between xiphoid cartilage and the left costal margin, the needle being directed backward and upward. There is probably less danger of going through the pleura at this point. A small aspirating needle about 2 inches (5 cm) long should be used, the greatest care being taken to insure an aseptic operation.

After the diagnosis of purulent pericarditis was confirmed, the patient was transferred to the surgical service. Examination of the chest at that time showed more marked signs of a pericardial effusion. The heart sounds were distant, the pulse fairly strong and the heart rate, about 140 and regular. The area of cardiac dulness at that time extended on the left side to the anterior axillary line, in the third, fourth and fifth interspaces, there was some enlargement to the right of the sternum. No murmurs or friction rub were heard. Thick mucous râles were heard over both lungs anteriorly and posteriorly. No areas of bronchial breathing were heard.

In the etiology of bronchiectasis, the following factors are commonly considered aspirated foreign bodies, kinks of the bronchi, pressure by aneurysm or tumor from without, growth in the bronchus, tuberculous or syphilitic stricture, webs, bronchitis, peribronchitis, bronchopneumonia and pleuritic infection, influenza and tuberculosis, occasionally pressure from enlarged lymph nodes is mentioned

In the young, the lymphatic system of the lung is "open," and the lymph nodes of the bronchial tree are probably affected in every case of infection of the lower respiratory tract, but in whooping cough, measles,



Fig 9 (case 4) —Roentgenogram showing the heaviest markings in the upper lobes and at the division to upper lobe bronchi on both sides. Arrow *a* indicates enlarged nodes in the left tracheobronchial space, arrow *b* points to abscessed nodes in inferior tracheobronchial space

influenza and tuberculosis the nodes seem particularly prone to become involved. Forgeron<sup>21</sup> reported twenty necropsies in children between the ages of 3 months and 5 years in which death was due to whooping cough in ten cases, to influenza in two, to diphtheria in one, bronchopneumonia in one, edema of the lungs in one, mixed infection with tuberculosis

<sup>21</sup> Forgeron, H. l'Adenopathie tracheobronchique simple chez l'enfant, These de Paris, 1922, p 191

*March 18* An acute suppurative otitis media developed in the left ear

*March 21* Thoracotomy was performed under local anesthesia, with removal of 3 inches (7.6 cm) of the eighth rib, posterior axillary line. A large amount of pus was evacuated.

*March 23* The pericardium was aspirated and 1,600 cc of thick greenish pus withdrawn. Culture of this pus showed pneumococcus, type II.

*March 25* The sixth and seventh left costal cartilages were removed under local anesthesia, the internal mammary artery was ligated, and the pericardium was exposed by blunt dissection. The heart was adherent to the anterior pericardial wall. An incision was made in the pericardium to the left of the adherent heart, and about 1,500 cc of pus was removed with a suction apparatus. As in case 2, irrigation was not carried out, and drainage material was not placed in the pericardium. The pericardium was sutured to the intercostal fasci and muscles. The wounds were dressed daily for five weeks, when both the empyema and the pericardial wounds were practically healed. About this time, swelling of the feet and legs developed and myocardial insufficiency was feared. The patient was returned to the medical service of Dr Shattuck who made the following notes:

*May 1* "Lungs—right posteriorly—from angle of scapula to base, dullness diminished; voice and breath sounds and bronchial breathing with occasional fine moist râles. Left, posteriorly—dullness and diminished breath sounds at extreme base.

Heart. Sounds are good, not rapid, regular.

Signs in chest show that there is still a considerable pathologic process, either unresolved consolidation, encapsulated or free exudate. Roentgenography or exploratory puncture of right side, particularly, needed to clear up the picture."

*May 3* The patient left the hospital against the wishes of the attending physicians.

*June 18* After the patient went home, the empyema wound opened, and considerable pus escaped. Drainage continued for about two weeks. Improvement was rapid and progressive from this time. There was considerable gain in weight and increase in stature, and satisfactory general development. When last seen and heard from, the boy appeared to be in perfect health.

*Summary*—1 In this case the suppurative pericarditis was secondary to a severe attack of double pneumonia, and complicated by a left-sided empyema. The infecting organism in the pericardial exudate was the pneumococcus, type II.

2 The pericardial effusion was discovered on the twelfth day, aspiration of 1,600 cc of pus was carried out on the twenty-fifth day, and pericardiectomy was performed on the twenty-seventh day of illness. The sixth and seventh left costal cartilages were resected in exposing the pericardium. The cavity was not irrigated, and drainage material was not placed in the pericardium.

3 Convalescence was protracted and stormy, but the patient eventually recovered.

#### COMMENT

Suppurative pericarditis, in my opinion, is never a primary disease. It is always a secondary or complicating infection of some lesion or lesions. It is usually due to direct extension of infection from the lung or from the lung and the pleura. It may follow wounds in the chest,

case 3, there were calcified nodes and pronounced fibrosis at the angle of division of the bronchi to the various lobes, and the enlarged (tuberculous) inferior tracheobronchial nodes in case 5 caused death by compressing the bifurcation and bronchi. The cases just mentioned indicate that, particularly in childhood, swollen lymph nodes, tuberculous or nontuberculous, may compress the bronchi as well as the vessels, the effect of such compression in the presence of infection may lead to bronchiectasis.

I wish to call particular attention to the bronchopulmonary nodes as potent factors in the causation of bronchiectasis in children. The lymphoid masses probably act in a similar way at the divisions of the smaller bronchi. When these nodes and masses are enlarged, inflamed and associated with periadenitis and edema, their position at the angles of division of the bronchi and bronchioli renders them peculiarly apt to interfere with the function of important structures. The nodes may compress the bronchi directly, or the fibrous tissue following the acute periadenitis may constrict the necks of the affected bronchi and prevent proper ventilation and drainage, the nodes may exert pressure on the vessels and give rise to congestion and edema, or the nerves may become affected by pressure or inflammation. It has been observed that periadenitis with edema surrounding the recurrent laryngeal nerves in the mediastinum has caused loss of function in the corresponding vocal cord, and that a similar cause in the case of the phrenic nerve resulted in insufficiency of the diaphragm. Therefore, it seems logical that a similar cause may have the same effect on the nerves of the lung. The nerve supply of the lung, according to Miller,<sup>22</sup> comes from the pneumogastric reinforced by branches from the second, third and sometimes the fourth thoracic ganglia of the sympathetic nerve, the nerves follow the bronchi throughout their course and are usually found associated with a branch of the bronchial artery in the layer of connective tissue which surrounds the bronchi. The bronchial musculature, as described by Miller,<sup>23</sup> provides for the elongation of the bronchi and bronchioli during inspiration and the shortening during expiration.

In extreme expiration the dorsal and lateral branches form an acute angle with the main stem bronchus, while in inspiration they open out, the angle becomes wider and at the same time they elongate. This change is necessary in order that provision may be made for the adequate expansion of the air spaces.

22 Miller, W. S. A Study of the Nerves and Ganglia of the Lung in a Case of Pulmonary Tuberculosis, *Am Rev Tuberc* 2 123, 1918.

23 Miller, W. S. The Musculature of the Finer Divisions of the Bronchial Tree and Its Relation to Certain Pathological Conditions, *Am Rev Tuberc* 5 689, 1921.

drained. The next two patients had streptococcic septicemia, and both died. In the fourth case the bacteriology was never clear. So far as the pericarditis was concerned, a smear was made from the fluid aspirated from the pericardium and many different kinds of organisms were found. I looked up the case recently, but I could not find a definite report on any culture. The patient died of septicemia. I do not believe that if a patient has a general septicemia and pericarditis, drainage of the pericardium will cure him. We all try this procedure, but it is hopeless.

I have always been interested in closed suction technic in certain cases of empyema, and I do not see any reason why it cannot be applied to pericarditis. In fact, I have used it. The case in which my patient recovered was presented at the Boston meeting of the Society in 1920. The patient was operated on by a closed suction method, a small catheter being placed in the pericardium cavity. This technic is based on the idea that it is the least severe operation one can perform. It does not allow air to enter the pericardium, which, I think, is probably a good thing. The catheter can be placed around the heart and into the posterior part of the pericardium, which is the point to drain.

Suction was the only postoperative procedure used in the case in which this technic was employed and in which the patient recovered. The catheter was shut off except when suction was being made. Irrigations were not used. Eventually, after four weeks, when practically no pus was discharged, and when this pus contained one organism to five or six fields, the catheter was removed. The patient recovered, he is well now after seven years.

Two other patients were operated on by this method. Both had streptococcic septicemia, and both died, which did not surprise me.

In the fourth patient, a costal cartilage was removed. It seemed to me that he had a small pocket of pus outside the pericardium and a large amount of pus in the pericardium. One or possibly two small rubber tubes were used for drainage. Irrigation with salt solution was instituted in this case and in one of the other cases in which the closed suction method was used. I could not see that the irrigation had any effect. I think that Dr. Pool's case, in which a surgical solution of chlorinated soda (Dakin solution) was used for irrigation, was striking. I do not see any reason why the solution should not be used.

DR. CARL A. HENMON, Chicago. The chief reason, in my opinion, for the frequent failure of physicians to diagnose pericarditis with effusion, at least in cases in which the condition is suspected, is the fear of an exploratory pericardiocentesis. If a large needle or a trocar is used, as detailed in many case reports, there is, I believe, some danger of injuring the heart or of producing hemorrhage, but a large needle is not necessary, and a trocar should never be used. In my experience, an ordinary medium-sized hypodermic needle, no. B-D, about 3 cm. long, is large enough, and, in my opinion, it does not involve any more risk than an ordinary exploratory aspiration of the pleural cavity. I have aspirated several hundred cubic centimeters of effusion at one sitting through such a needle.

An early positive aspiration will establish the differential diagnosis and will determine early treatment.

One of the possible sources of error is to assume that there is no pericardial effusion from one dry tap. The usual point for inserting the needle, as Dr. Peterson says, is at the left of the sternal margin. It has been shown, however, by Williamson and others, that the heart may be pushed forward

Röntgenograms showed that the right lung contained less air than the left, particularly the upper lobe, and the left upper lobe was more cloudy than the lower lobe (fig 10). Enlarged bronchopulmonary nodes were seen, some were calcified. The mediastinal shadow was broader than normal in the upper right part. The right main bronchus seemed to be at almost right angles with the trachea. There was a large triangular shadow below the bifurcation and the main bronchus no foreign body was seen. Bronchoscopic examination revealed some edema of the epiglottis. The lower wall of the right main bronchus and the corresponding part of the bifurcation appeared as if pushed upward, causing



Fig 11 (case 5)—Roentgenogram of necropsy specimen. Abscess cavity is indicated by *a*, displaced esophagus injected with barium mixture by *b*, trachea by *c*, and right bronchus by *d*.

considerable narrowing of the lumen of the right bronchus. The mucosa was red and edematous. A foreign body was not seen. Culture was taken from the bifurcation through the bronchoscope. The diagnosis was infection and enlargement of the lymph nodes in the inferior tracheobronchial space compressing the right main bronchus and the bifurcation. The child died two days later.

Necropsy revealed an enlarged thymus gland to which several enlarged lymph nodes adhered. There were some enlarged preaortic nodes, and the eparterial group was considerably enlarged. The nodes of the left tracheobronchial group were small and soft, while the right group formed a firm, somewhat flat mass,

amount of old blood coagula were removed by irrigation, prolonged drainage followed. The patient recovered and his wound healed, when I saw him he was in good condition.

One physician does not usually see a large number of these cases, yet they are frequently found. My personal opinion accords with that of Dr Hedblom, i. e., that aspiration should be performed when there is an enlarged shadow of the heart much oftener than is done in the medical ward. Why not also plunge the aseptic needle into the pericardium as we know every physician does with reference to the pleural cavity? If he does not want to do it himself, let him call a surgeon. Certainly many patients with acute infectious diseases could improve considerably if simple aspiration were performed repeatedly, if necessary.

Regarding surgical treatment, personally, I can never forget what I might call the thrill I had at our Boston meeting when Dr Whittemore told us of the case in which he saved a boy, aged 12, who had influenza with complicated pericarditis. I have always believed in the correctness of closed drainage after intrathoracic operations. That was the guiding thought several years ago at the Lenox Hill hospital, when Dr Pickhardt and myself and members of the staff, discussed the best treatment for empyema according to the experience gained from air-tight drainage after thoracic operations. We came to the conclusion that it would be best not to plunge in the trocar as we had done a number of times according to the old Bulau method of the last century, which had shown brilliant results at times, but that we should do the work under the guidance of our eyes. We selected the following method. Under local anesthesia, we resect as long a piece of the rib as one can, then make as long an incision as possible in the posterior fold of the periosteum of the rib, and the appearance within is noted. Then, under the guidance of the fingers, and through a stab wound, the drainage tube is placed farther down, or 2 inches (25 or 5 cm.) from the diaphragmatic surface. This done, we close the entire chest wound in layers, making it air tight. We have had splendid results with this procedure. Dr Pickhardt told us at the Chicago meeting of this Society of his series of patients who had been treated and cured according to this so-called "physiologic drainage empyema." In the course of years, we have repeated this operation, and recently I was particularly interested in a brilliant textbook on children's diseases by Frazier of Edinburgh in which he published about seventy cases in which this kind of physiologic drainage was used with most satisfactory results.

I believe that many patients on whom thoracic operation is performed recover more easily, as they sometimes do in the hands of experienced men, if in the majority of cases the simple air-tight drainage would be added for forty-eight hours.

With this and with Dr Whittemore's brilliant personal experience in mind, I firmly believe that the closed method of pericardial effusion will probably prove to be the best. I believe this still more firmly since I had the opportunity of observing two acute cases that occurred in the hospital while I was still in active service. One patient was operated on by Dr Pickhardt and one by myself. We used open drainage method, both patients died. I decided that if I should ever have a case again that required this kind of operation, I would not use the open method of after treatment, particularly in adults. I think there is a difference between the treatment required for adults and children. I would use the method of open incision close to the sternum as possible and thoroughly remove the coagulated material in the pericardium, I would then know that after suction the sac was as clean as was possible. I

smoothly in the knife-carrying tube, and this tube fits snugly in its channel in the bronchoscope. The proximal end of the shank to which the handle is attached is flexible, so that it can be worked out of the way. The depth of the puncture must be considered beforehand, as it

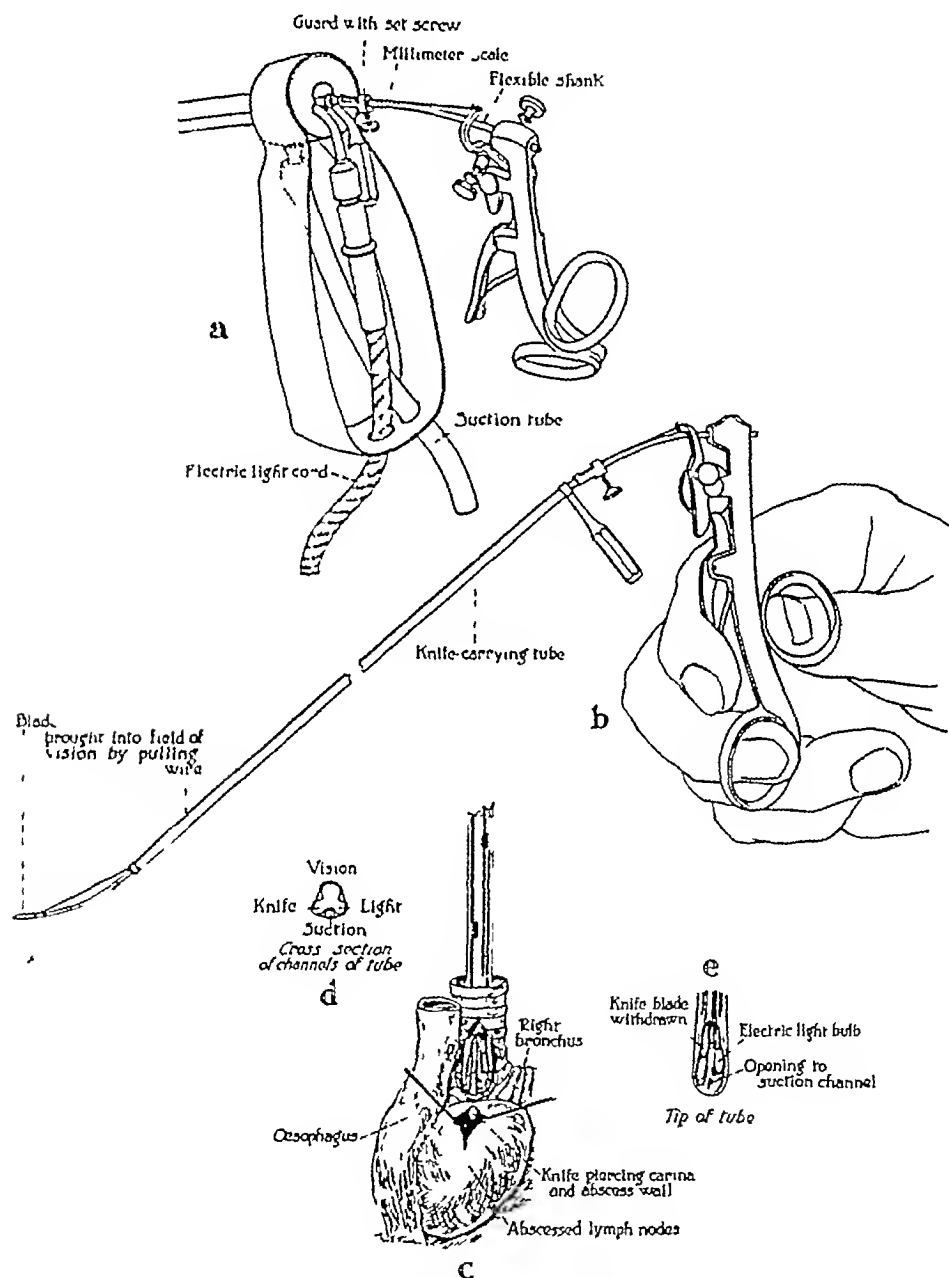


Fig 12 (case 5) —Bronchoscope used by the author and instrument for "puncturing" abscess of the tracheobronchial lymph nodes

will depend on the thickness of the bronchial wall and on the anatomic relations in the area to be punctured. The thickness of the tracheal wall when the patient is from 1 to 2 years of age is 0.17 cm, when he is from 15 to 16 years, it is 0.22 cm, therefore a puncture from 0.2 to



Two transfusions were given according to the Lindemann method, and the patient finally recovered. It is possible that the transfusions did not do any good, but I think it should be borne in mind that transfusion is a notable aid toward recovery from *Streptococcus hemolyticus* infection of the blood.

DR HOWARD LILIENTHAL, New York. I have had experience with four patients—two recovered and two died. One of the patients who died, a little child with empyema and septic pericarditis was operated on, the other patient had actino mycosis with secondary infection of the pericardium caused by unskilful puncturing with the needle. The pericardium was entered, and this produced pericarditis. The patient died of the disease, whether of pericarditis alone or not, I cannot say.

The problem of closed suction is a totally different one in pericarditis from suction in drainage of the pleura. Closed suction in the pleura is intended to produce a rather prompt dilatation of the lung, bringing it to the surface and obliterating the pleural sac. There it is justifiable. I cannot see the advantage of it in the pericardium, but I can see many disadvantages. If one should wish to perform lavage, it is extremely dangerous to irrigate through closed suction. Patients have died as a result of this. In a case of Dr Herman Roth, the patient collapsed and almost died before Roth found out what the trouble was and pulled the tube out, the patient revived. His fingers had relaxed, his pupils had dilated, his heart had stopped and breathing had ceased but returned with removal of the tube.

The problem is a totally different one from that of empyema. In fact, in the older operations for pericarditis, some of which were successful, the pericardium was deliberately held open. I have always sutured the pericardium to the skin or to the superficial tissues to maintain potency. An advantage of this is that one can reach in with a probe or soft rubber catheter and get to the posterior sac of the pericardium, making sure that it is empty. The pericardium acts exactly as the rest of the chest so far as respiration is concerned. With a respiratory effort like cough, the walls of the pericardial sac as well as the pleural walls, are forced together, and there is extrusion of fluid with suction on in aspiration.

It has been suggested that diagnostic aspiration may safely be made from behind, and it has been performed in one or two instances. I wish to warn against this. There is too much danger of infecting the mediastinum with pus from an infected pericardium to make it worth while except in a case of hydropericardium in which aspiration is performed for relief, in that case it is easy enough to get at it from in front.

I strongly disapprove of the closed suction methods in pericarditis, even though we have heard a report by Dr Whittemore of his successful case. I should like to hear the results of a series of these successful cases before I should care to change my mind.

DR ROBERT T MILLER, JR, Baltimore. I have had two cases of this kind. The only reason for speaking about them is that they seem to be unusual. The first occurred a little over eighteen years ago. The child had suppurative pericarditis complicating scarlet fever. Resection of the fourth and fifth left cartilages was performed. When the wound was dressed the pericardium was irrigated until the returning fluid became clear, following which a rubber protective tissue drain was inserted into the pericardial sac. The child died in spite of all efforts, his death was apparently the result of loss of blood from the wound—a loss of blood which in a way suggested hemophilia. He did not bleed in large amounts, but there was a continual loss of blood which

calcification are often seen peripherally in the lung, beyond the area of the lymph nodes, and these points of calcification may be the results of healed inflammatory processes in the lymphoid masses

I wish to make a plea for the use of the terms "tracheobronchial" nodes and "bronchopulmonary" nodes, instead of hilum nodes, bronchial nodes at the root of the lungs and other terms

#### ABSTRACT OF DISCUSSION

DR ALAN WHIPPLE, New York I have always followed Dr Lerehe's studies of the arrangement of the lymphatic system in the mediastinum with great interest I am pleased to see that he is still pursuing the subject and has brought out the effects of enlargement of the bronchial nodes, particularly in children, on the development of bronchiectasis It seems to me that is a logical sequence of events as he outlined it

Dr Lerehe has emphasized especially the role of pulmonary infection in its relation to the involvement of the tracheobronchial and bronchopulmonary nodes That is of special interest to the thoracic surgeon On the other hand, I think there is a phase of it that is just as interesting, and from the standpoint of the general surgeon is even more important, i e, the involvement of the mediastinum following abdominal infections

I wish to stress that feature of it particularly and will take a short time to discuss it

In the last three or four years, I have seen four cases that impressed me particularly as cases of infection of the mediastinal lymph node following abdominal lesions A man came to me with the history of severe cholangitis He recovered from it, when suddenly his temperature rose and he became prostrated He was sent to me with a diagnosis of cholangitis without jaundice, however In going over the records concerning the man's physical examination, I was much impressed by an area of dullness situated to the right side of the sternum, with signs posteriorly as well During the examination, he suddenly began to cough and coughed up foul pus He was taken immediately to the fluoroscopy room and a collection of fluid was clearly outlined to the right of the sternum, in the mediastinum, causing a definite blocking of the postpericardial shadow There was a fluid level, and it seemed to be a case of mediastinal abscess breaking through into the bronchus Bronchoscopy was not performed, but the patient continued to cough up pus, in a few days, he was much better, and he recovered from that attack During his convalescence, he went to California, and on his way back through the Panama Canal, he had a recurrence of bile duct infection He arrived in New York with severe cholangitis An operation was performed, although at the time the man showed a continuance of the shadow to the right of the sternum He died from severe postoperative pneumonia I think that the infection had passed through the diaphragm into the mediastinal lymph nodes and had resulted in an abscess which broke through the bronchus, and that there was a continuing line of infection between these two structures

Another case was one of streptococcus infection Beginning as peritonitis, a double empyema, a left subphrenic abscess followed At the time I was taking care of the boy, the same shadow developed to the right of the sternum The infection did not break through the bronchus and the boy recovered

The other two cases are similar, and I will not take the time to describe them, but I want to stress this There are three kinds of mediastinal infection

Dr Ellsworth Eliot There have been about five cases of suppurative pericarditis within the past few years but the patients were adults It would almost seem that children are the ones who have a fair chance of recovery and that the mortality rate of adults is much higher In diagnosis, I think it is of interest to note the unaccountably rapid pulse rate that occurs with pericarditis in marked contrast to the temperature A much more delicate test is possible with the aid of a blood pressure machine By this method, one may listen around the upper limits of the systolic pressure and may note when the first sounds come through on expiration The number of millimeters of mercury registered by the blood pressure machine at the time when the sounds first come through on expiration should be noted The same notation should be made at the time when the sounds are heard equally well on inspiration and expiration The difference in millimeters of mercury between these two registered pressures may be greatly increased over the slight difference that may normally occur If that range is a high one, it is a clear-cut indication of the paradoxical quality, and has been present in all the cases that I have seen In one case it was interesting to note a complete disappearance of a marked paradoxical pulse on aspiration

The aspiration externally appeals to me, as Dr Hedblom remarked, internal to the outer margin of the dulness and external to the apex All of the patients on whom it was necessary for me to operate died They were all adults The last case was caused by type III pneumococcus A wide open type of operation was performed similar to the one recommended by Dr Pool The patient lived for three weeks after a wide open exposure As the operation was performed under a local anesthetic, it was possible to push the pleura back and make a wide opening in the pericardium and stitch it to the skin When a clamp was placed on the pericardium at its junction with the diaphragm, the patient complained of pain in the left shoulder That was in the region of the fifth and sixth rib, as Dr Lord brought out A surgical solution of chlorinated soda (Dakin solution) was used in this case part of the time It was possible to pass a catheter to behind the heart and to introduce a finger between the heart and diaphragm and toward the apex with little, if any, effect on the patient Suction drainage was also used part of the time The patient had extensive lesions elsewhere She had an enormous abscess of the thigh and infection of the knee joint caused by type III pneumococcus At the autopsy, adhesions were found, but there was no accumulation of pus in the pericardial sac, and the pleural cavity was clear

Two or three other cases that we have had have led us to consider the possibility of drainage by the posterior route in pericarditis, particularly if the pericarditis is associated with left empyema We have been looking for a case in which the left side of the chest is involved with an empyema so that the approach to the pericardium can readily be made through the pleura I saw one case without empyema with Dr Whipple, which I think he has reported He made a posterior incision of considerable extent, near the diaphragm, avoiding the phrenic nerve The pericardial drainage in this case appeared to be satisfactory, though the man died after living several weeks

It is striking to see how close the pericardium is to the wall of the left side of the chest when distended with fluid I have had occasion to see that at autopsy, and to see how close to the wall the pericardial sac actually is in the region of the seventh and sixth spaces It seems as though one has to travel a short distance in making a posterior lateral incision in order to enter the pericardium at the site that would seem to be the most favorable

broncholiths are removed, the patient is likely to continue to have the symptoms of chronic pulmonary suppuration, when the last broncholith has been removed, the patient will usually recover. One patient has expectorated as many as 126 broncholiths over a period of six months. Some of these are exceedingly small. I have a feeling that as Lerche expressed it, the origin of many is in the tracheobronchial glands. The patient is not likely to get well until all of the broncholiths are discharged.

DR L. T. LEWAND, New York. I should like to emphasize one point that Dr Lerche brought out, that is, that following infectious diseases of childhood bronchiectasis occurs. One of the last things the late Dr Lynah did was to have established a roentgen-ray department at the Willard Parker Hospital, one of the largest hospitals in the country for the study of contagious diseases. I was asked to direct the work there. There were immediately a number of cases of children who had had postdiphtheritic stenosis of the larynx. Bronchiectasis was common, and one case particularly was interesting because the bronchiectasis was in the upper lobe. Dr Lerche is correct, I am sure, in saying that bronchiectasis occurs early in life following the infectious diseases.

Beginning this year at the Willard Parker Hospital, we hope to make roentgenograms of all patients as they come into the hospital and before they leave, possibly we can also establish a follow-up. In a year or so we will be able to report the results of that work.

DR LERCHE. I forgot to mention one thing, namely, that the lymphatics of the inferior half of the lower lobe do not drain into the tracheobronchial nodes but into preaortic nodes which may be of clinical importance.

# LIPOMAS OF THE MEDIASTINUM\*

EVARTS A GRAHAM, M D

AND

E R WIESE, M D

ST LOUIS

The tumors of the mediastinum which are supposed to be most common are readily recognized by the roentgen ray. They include the various neoplasms involving the mediastinal glands, substernal thyroid adenomas, aneurysms, dermoids and other tumors. In the case of the lipoma, however, a shadow is not revealed unless it is large. It has occurred to us, therefore, that fatty tumors may actually be much more frequent than the few references to them in the literature would indicate, especially since it might be easy to overlook them at postmortem examination unless they were unusually large. Their clinical importance lies in their ability to produce effects of pressure, and they should be considered as possible causes of symptoms in those cases in which there is perhaps an otherwise unexplained choking sensation, a recurrent laryngeal paralysis or similar condition. Our attention was attracted to these possibilities by a recent case.

## REPORT OF CASE

B N, a white man, aged 43, of strong physique, was admitted to Barnes Hospital because of a small mass in the lower right side of the neck. He had first noticed it about six months before admission. Shortly afterward, he began to have intermittent choking spells with dyspnea of short duration. A little later, attacks of pain occurred which began in the neck and traveled downward on the right side into the chest. The choking sensations seemed worse during the attacks of pain, and at these times he observed cyanosis of the finger tips. There had also been indefinite attacks of numbness of the right arm and of the right side of the chest. During the last few weeks, he had noticed hoarseness which at times was severe. The lump in the neck had gradually grown larger.

Examination revealed a soft diffuse swelling above the sternum, more on the right side than the left and apparently coming up into the neck from behind the sternum. This mass was movable, not tender, moved only slightly on swallowing and did not pulsate. Substernal dullness was not present on percussion. On forced inspiration, the mass came up higher in the neck. Laryngoscopic examination showed that both vocal cords moved, but the left seemed to override the right slightly. Roentgen-ray examination revealed nothing of importance except that there was an abnormal upward bulging of the right leaf of the diaphragm in its middle portion. There was no obstruction of the esophagus. Examinations of the urine and blood revealed nothing abnormal. The Wassermann reaction was negative. The pulse, temperature and basal metabolism were all normal.

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In the course of the deliberations in Chicago, negative pressure was declared to be the best adjuvant for safe operating within the thorax from a physiologic as well as a pathologic point of view, though positive pressure for the exclusion of a possible collapse of the lung also had its advocates. The hope was expressed that with further investigation this fundamental question would be definitely solved in the near future.

Soon a negative chamber was built in New York, and having been tested in animal experimentation, it was erected in the thoracic pavilion of the German Hospital, later renamed the Lenox Hill Hospital, of New York City. It permitted the changing at will from negative to positive pressure and vice versa, without the necessity of moving the patient, instruments and everything else from the inside to the outside of the chamber or vice versa, as had been necessary for such a change of pressure in the older chamber models. The New York chamber had been built in this way for the purpose of determining in as scientific a way as possible the relative clinical value for the patient of the two types of air pressure, negative and positive. The chamber also allowed the production of prolonged artificial respiration with the greatest ease, by simply moving a valve handle to and fro.

While this New York chamber was being experimentally constructed, tested and rebuilt and erected for clinical work, a number of new apparatus for positive pressure only were tried extensively. Conspicuous among them were Brauer's and Robinson's box, Brat-Schmieden's and Tiegel's mask apparatus—the latter surgeon proving as early as 1908 that 1 mm. of pressure of pure oxygen suffices to avoid the deleterious accumulation of carbon dioxide in the blood after acute collapse of the lungs—the Meltzer-Auer intratracheal insufflation and Branower's pharyngeal insufflation.

In consequence of the rapid evolution of thoracic surgery resulting from all of these new devices, the scientific investigation for which the New York negative chamber had been constructed was never carried out in a series of cases. Clinical observation in operations performed under positive pressure, with the employment of Tiegel's oxygen pressure apparatus abroad and intratracheal as well as intrapharyngeal insufflation in America, proved in phenomenally quick succession that such carefully conducted observations were not needed.

By this time the World War had begun, and it soon focused the attention of the medical profession at large on thoracic surgery. Surgeons returned from the front with the message that intrathoracic operations could be performed without apparatus for the control of air pressure. The experiences gathered during the war, however, could not shake the firm pillars on which the building of modern thoracic surgery had been erected. After repeated and thorough discussion, particularly in our association, it was resolved unanimously at our meeting

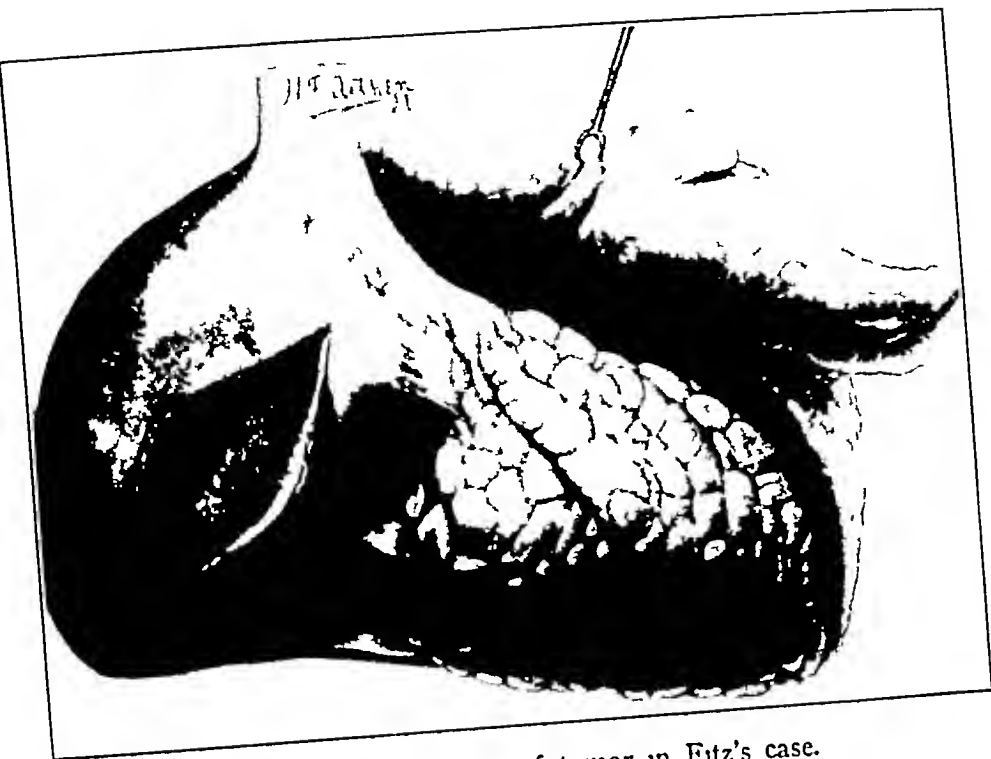


Fig 2—Appearance of tumor in Fitz's case.



Fig 3—Drawing made at operation in author's case

time, restored the heart action to such an extent that any other intervention became superfluous. On the other hand, when the hospital no longer had the negative chamber and the plus-pressure cabinet, I lost a patient with a large pulmonary lip-fistula and marked bronchiectasis of the left upper lobe, whose lung, because of repeated severe hemorrhages was being collapsed in stages. The patient died because we were unable to keep the mask on his face for the long period required. But it was again clearly shown that breathing pure oxygen under pressure with the mask in place restored the failing heart as long as it could be kept up.

Personally, I feel that the lack of such an apparatus at the Lenox Hill Hospital at the present time represents a defect in the armamentarium for the proper after-treatment in certain cases. I am pleased to add, however, that the chief of the division of anesthesia has in mind the construction of a breathing device of the type described.

From a broad point of view, thoracic surgery is today able to bring help whenever required. With the special operating room eliminated, with thoracic operations, like all others, performed in the general operating room and with acute pneumothorax overcome by simple means, every nook and corner within the chest can be safely reached, in one word, the thorax is as wide open for aseptic surgery as the abdomen has been for almost fifty years. There are no more pitfalls or unexpected snags to mar the results of the experienced surgeon's fascinating work.

The evolution of the principles of thoracic surgery is complete. It has reached a status of which surgeons the world over—and all nations have done their share in attaining this goal—may well be proud, this is an inspiring retrospect. What remains to be done is to study the details further and to work out to perfection methods for thoracic operations, as has been done for operations on any other part of the body.

Nothing contributes more to progress in any field than free discussion by the men interested. Our association was founded ten years ago solely for this purpose, and free and unlimited discussion at the annual meetings is an absolute necessity. A limitation to five minutes for each discussor seems inadvisable. We all want to learn from the most recent experience of our colleagues.

Now, what is the outlook for thoracic surgery in America with its vast areas and enormous distances? Patients chronically ill but transportable, will naturally not mind the distance, they will consult the experienced surgeon of their selection, as they have done heretofore. But what about these acutely ill, the large number of those injured by automobiles by train collisions and by accidents and explosions in factories, who have sustained internal injuries of the chest? And what about patients with fulminant inflammation, acute gangrene of the lungs and other conditions for which they need prompt and adequate treatment lest they die? In the large cities with a multitude of



In 1887, Kronlein<sup>2</sup> reported a case in an infant, aged 6 months, in which the operation was performed by Langenbeck. A tumor presented, extending from the right axillary line to 3 cm beyond the left sternal edge and from two fingerbreadths below the right clavicle to the xiphoid cartilage. The tumor was exposed and found to continue into the chest through the third intercostal space by a pedicle. The pedicle was cut across and the external tumor removed. The child died of erysipelas, and autopsy revealed a rounded lipoma as large as a child's head, which was covered with a firm fibrous capsule and which filled the anterior mediastinum. In 1892, Gussenbauer<sup>3</sup> reported the case of a woman, aged 42, who presented a tumor at the upper border of the left breast, it was painless and at first was about the size of a nut. It grew steadily and three years later, the patient came to operation. A pedicle about twice the size of a finger extended into the chest through the second intercostal space. The intrathoracic portion was enucleated and removed. It was a little smaller than the outer tumor, about the size of a man's fist. The entire tumor was about twice the size of a fist. The patient recovered. In 1905, Fitz<sup>4</sup> reported before the Association of American Physicians a case of a man, aged 34, who died of acute pericarditis. At autopsy a mass of fat about the size of the head of a newly born infant, shaped like a pear, was found attached to the pericardium on the left side and continuous with the fatty tissue of the superior mediastinum. The mass was divided into lobules by connective tissue and projected into the inferior and anterior portions of the left pleural cavity. It was adherent to the diaphragm, pericardium, parietal pleura and the left lower lobe. In spite of the large size of this mass, symptoms ascribable to it evidently had not been present. In a discussion of this case at the same meeting, Ewing described a lipoma which had been found in the dissecting room in the body of a man who had died of acute lobar pneumonia. A large, lobulated mass of fat was found in the anterior mediastinum, this mass sprang from a pedicle which ramified in many directions and involved the pericardium, passed up along the bronchi, trachea and great vessels which it partly surrounded and apparently infiltrated the diaphragm. In all these places there were bands or small lobulated fatty masses. The main part consisted of five lobules, each about the size of a goose egg. Both lobes of the left lung were diminished in volume by these masses which were packed together in the lower part of the left pleural cavity. In 1923, Beyers<sup>5</sup> reported a

2 Kronlein Arch f klin Chir (supp) **21** 157, 1877

3 Gussenbauer Ein Beitrag zur Kenntniss der subpleuralen Lipome, Arch f klin Chir **43** 323, 1892

4 Fitz, R H Intrapleural Lipoma, Tr A Am Phys **20** 57, 1905

5 Beyers, C F Case of "Subpleural" Lipoma in a Child, Lancet **1** 283, 1923

So it is the hope, and seems to be the proper outlook, for thoracic surgery in America, that in every state of the Union the accidentally internally injured person will find nearby a well equipped hospital prepared to help at a moment's notice, where a condition will be diagnosed correctly and where patients with acute inflammatory conditions of the organs within the chest will be treated scientifically. This hospital should have at its disposal the able cooperation of specialists in bacteriology, radiology and peroral endoscopy of the bronchial system and of the esophagus.

The time will soon come when, in the absence of the chief of the surgical staff of the smaller hospitals, the house surgeon or the medical assistant must be able to recognize the increasing pressure of accumulating air and blood within the chest, for instance, in the presence of a broken rib (or ribs), a piece of which has pierced the lung and allows the entrance of air into the pleural cavity or into the mediastinum with each inspiration without giving it a chance to escape. In a short time, the increasing "pressure pneumothorax" will extinguish life. The air-tight introduction of a small rubber drainage tube through the cannula of a trocar, pushed into the chest, and its easy connection with a syphon bottle under the operating table and bed may help the patient through the gravest moments and may even save his life. The same result will be attained by the comparatively simple operative entrance into the chest between the ribs in order to stop an uncontrollable active hemorrhage and to mend the tear of a lobe of the lung, or the bronchus, then the typical air-tight drainage of the pleural cavity should be instituted for the first forty-eight to seventy-two hours.

These life-saving principles of thoracic surgery after acute injuries should be taught in all medical schools. Every medical man who lays claim to the title "surgeon" should be prepared to enter the thorax and follow up a stab wound or a shot wound of the chest through the diaphragm into the abdomen. This will often suffice when it is necessary to stitch, remove or drain an injured spleen or kidney, to close a wound of the stomach within the dome of the diaphragm or to deal properly with a wound at the convexity of the liver with the help of the thoracic entrance alone or by a combined operation.

It is unnecessary, before this Association, to enlarge further on what has just been said. The aim is to have every medical student taught the principles of thoracic surgery. Let the enthusiasm of youth be kindled for this fascinating chapter of medical science! Then a still larger proportion of patients with foreign bodies in the bronchi or the esophagus, accompanied by acute intrathoracic inflammatory conditions, who may become crippled for life or die in the absence of prompt competent treatment, will be restored to their normal physical and economic status, and many persons injured internally, who at present die, will be saved.

# DIAPHRAGMATIC HERNIA

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An increasing number of cases of diaphragmatic hernia are being recognized, and the condition is probably more common than even present records would indicate. The condition is of interest to the surgeon because operation is being performed in a larger number of cases with satisfactory results. Undoubtedly more cases will be considered surgical as the indications for surgical intervention and the technic of operative procedure become more definitely established.

Ambrose Paré is credited with having described the condition in 1610. He reported two cases of traumatic origin. Riverius reported a congenital case in 1698. Kirschbaum reviewed seventeen cases in 1755. Morgagni wrote a monograph on the subject in 1769. Sir Astley Cooper discussed the subject in 1824. Bowditch reviewed eighty-eight cases in the literature up to 1886. Ricolfi, in 1886, reported an operative cure of a stab wound of the diaphragm through which the omentum prolapsed. Naumann, in 1888, operated in the first case of diaphragmatic hernia in which the hernial contents did not prolapse through the thoracic wall. Marana, in 1893, operated successfully in a case of stab wound with injury of the stomach which was detected by the finding of gastric contents in the thoracic cavity. In the same year Amante successfully repaired a stab wound of the diaphragm.

The roentgen ray with opaque mediums to outline the abdominal viscera has proved the most valuable diagnostic aid in the recognition of diaphragmatic hernia. The technic of this diagnostic procedure was fairly well standardized by 1908. According to Arnsperger,<sup>1</sup> diaphragmatic hernia had not been recognized in life more than ten times previous to 1908. In 1912 Giffin<sup>2</sup> reported 690 cases of diaphragmatic hernia of which only fifteen had been diagnosed clinically. In 1915, Kienboeck,<sup>3</sup> in a review of German literature, noted records of only three cases of diaphragmatic hernia and one of eventration which had been diagnosed in life and confirmed at necropsy. The reported incidence varies greatly

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1 Arnsperger, quoted by Unger, A. S., and Speiser, M. D. Congenital Diaphragmatic Hernia, with a Report of Seven Cases with Autopsies, *Am J Radiol* **15** 135, 1926.

2 Giffin, H. Z. The Diagnosis of Diaphragmatic Hernia, *Ann Surg* **55** 388, 1912.

3 Kienboeck, R. Ueber Megengeschwüre bei Hernia und Eventratio Diaphragmatica, *Fortschr a d Geb d Rontgenstrahlen* **21** 322, 1913-1914.

ligated, and the pericardium was exposed by blunt dissection, seized with clamps, brought forward and opened. Pus was forced out under great pressure for a distance of several feet. The pericardium was irrigated with saline solution, and rubber tissue drains were inserted into the pericardial sac. The immediate relief following operation was striking. The next day, however, there was a decided increase in the lung signs, and thirty-six hours after operation the infant died.

*Summary*—1 In this case the suppurative pericarditis was secondary to pneumonia.

2 A roentgenographic examination, about the sixth week of illness, showed a pericardial effusion. Aspiration of the pericardium by Dr. Dennett showed that the effusion was purulent. The infecting organism proved to be *Bacillus influenzae*.

3 Pericardiotomy was performed two days after the aspiration.

4 Relief was only temporary and death occurred about thirty-six hours after operation.

The report of the following case up to June 25 is modified from a statement by Dr. Adolph G. De Sanctis.

*CASE 2—History*—Lena C., aged 3½ years, was admitted to the babies wards of the New York Post-Graduate Hospital on June 14, 1922. This patient was referred to me by Dr. De Sanctis. The chief complaint was, according to the mother, an elevated temperature which had been as high as 104 F., and which had been continuous for two weeks previous to admission to the hospital. The family history was negative. The child had had measles, mumps and whooping cough. There was no history of diphtheria, scarlet fever, tonsillitis or rheumatism. She had been ill for two weeks prior to admission and had had a daily temperature varying between 100 and 104 F. The mother said that the onset followed a blow on the head with a stone. There was no apparent injury from the stone. Five days prior to admission she had had a generalized convulsion lasting twenty minutes but none had occurred since then. Her appetite had been poor, she had had one watery greenish stool daily, and had vomited a small amount occasionally. She had had a slight cough since the onset of her illness.

The important facts in the history were the elevated temperature and the history of the cough. There was no doubt that the fact that the child was hit on the head with a stone was a coincidence. The convulsion was probably due to the extremely high temperature at that time.

*Physical Examination*—The patient was a well nourished child and appeared to be acutely ill. Scars or evidences of external injury were not found on the scalp.

The teeth were in fair condition, the throat was slightly reddened and the tonsils were enlarged and cryptic. The neck was normal. The chest was symmetrical and respiration appeared to be equal on both sides.

The lungs were normal on palpation and percussion. There was a small area anteriorly just outside the left nipple, where the breath sounds were bronchial. Râles were not heard over any part of the chest. Posteriorly, the chest was normal.



On June 25, with the child in a semisitting posture on account of dyspnea, the operation was performed under local anesthesia. The left sixth costal cartilage was resected, the internal mammary artery ligated and the pericardium exposed without opening the pleura. The pericardium was seized with fine clamps and opened. Thick pus escaped under pressure. The remaining pus was aspirated with a suction apparatus, such as is used in operations on the throat. The pericardium was sutured to the wall of the chest. Drains were not used. Following evacuation of the pus, there was marked improvement in the patient's general condition. In order to secure good drainage, the child was made to lie face downward for a period of thirty minutes, every two or three hours. The patient cooperated well and gravity drainage of the pericardium was secured from the start. The wound healed completely in about one month.

On July 20, an electrocardiographic study was made. The time relations and deflections indicated that there was no heart block in any area. The auriculo-ventricular rate of the heart was 132 a minute, the rhythm, regular. There was no intermittence. The "T" deflection was inverted in lead II and flattened in lead III. This is seen only in abnormal hearts, but the significance is uncertain. The record is not typical of that of "congenital heart." If hypertrophy is present, both ventricles are equally affected, because the records do not show preponderance of either ventricle.

*Summary*—1 In this case the suppurative pericarditis was secondary to pneumonia.

2 Roentgenographic examination of the chest, on the twenty-second day of the child's illness showed a large pericardial effusion. Aspiration of the pericardium by Dr. De Sanctis on the same day showed that the effusion was purulent. Culture of the pericardial pus showed the infecting organism to be *Staphylococcus albus*.

3 Two days later, pericardiotomy was performed. The sixth costal cartilage was resected. About 750 cc of pus was removed by suction. The pericardium was not irrigated and drainage material was not placed in the pericardial sac. Postural treatment was depended on to accomplish drainage.

4 The wound healed completely in about one month. At the present time the child appears normal and healthy. There is, however, a slight systolic murmur of the heart, heard at the apex, but not transmitted to the back.

*CASE 3*—MAN, S., aged 14, was admitted to the service of Dr. Shattuck at the New York Post-Graduate Hospital on Feb. 28, 1924, with a temperature of 105.6 F., respiration, 40, pulse rate, 140. Two days before the boy had had a chill, headache, sharp pain in the left side of the chest, cough and vomiting and had expectorated bloody sputum. A diagnosis of lobar pneumonia of the lower lobe of the left lung was made. The boy was profoundly toxic and critically ill for about two weeks. He was in the hospital for over two months and during the greater part of this time the course of his illness was stormy. Only the most important features of his illness are given here.

*March 1* Examination of the sputum showed influenza bacillus and type IV pneumococcus.

*March 10* There were signs of a pleural exudate and of marked increase in the total area of the heart. A roentgenogram showed an effusion in the left side of the chest and a large pericardial exudate.

*March 13* Thoracentesis was performed of the left side of the chest, and 130 cc of turbid serum withdrawn. The chest was aspirated again on March 13, 16 and 19. At the last aspiration, the fluid had become frankly purulent.

and bears a definite relation to esophageal hernia. About this period (11 mm) a physiologic alteration in the abdominal area takes place. The celom has not increased in size enough to take care of the rapid changes that are taking place within its walls and which are augmented by the descent of the septum. As Mall<sup>11</sup> states, "Since the liver grows downward and crowds upon the rapidly elongating intestine, the intestine must escape it if it has a chance and the coelomic space within the umbilical cord naturally receives it." This phenomenon, known as the physiologic umbilical herniation, provides a reservoir for the abdominal contents until the peritoneal cavity has grown sufficiently to store its own contents. The herniated intestine is restored to the abdominal cavity by the growth of the abdominal wall past the fixed mesentery of the intestines.\* This physiologic herniation starts at 11 mm, is well developed at 22 mm and starts on its way toward voluntary reduction at about 35 mm.

During this period of greater activity in the abdominal celom, the diaphragm is incompletely formed, and the hiatus pleuroperitonealis is patent. The closure takes place on the right side first at about 17 or 18 mm and on the left side at about 19 or 20 mm. The left side of the liver has largely disappeared, and the whole organ has rotated to the right and fused with the right wall of the body, protecting to a great extent the right half of the diaphragm and probably aiding its more rapid completion. The stomach has reached its permanent site below the diaphragm before the left half of the diaphragm is closed. Therefore the hiatus pleuroperitonealis patent on the left side is in direct contact with the rapidly forming and constantly changing hollow viscera during this period of physiologic umbilical herniation.

It would seem that this time of the incomplete closure of the diaphragm in relation to multiple rapid changes which are taking place in the embryo is of great importance in the preponderance of left-sided congenital defects. To recapitulate, these changes consist of (1) the occurrence at this time of the normal physiologic umbilical herniation, (2) the patency of the hiatuses connecting the peritoneal and pleural cavities, the left closing last, (3) the sudden descent of the diaphragm, which is considerably in advance of the descent of the stomach, (4) the shift of the liver to the right because of anchorage and the degeneration of the left lobe from vascular change and pressure, (5) the presence of hollow mobile viscera on the left side, (6) the elevated position and smaller size of the left lung, (7) the rotation of the stomach to the left and (8) the presence of bursae at the esophageal opening.

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11 Mall, F. P. *Manual of Human Embryology*, Philadelphia, J. B. Lippincott Company, 1910-1912, vol. 2, p. 321.

it may complicate a distant focus of infection, such as an osteomyelitis, and it may be part of a general sepsis. Such being the case, the prognosis will depend, to a considerable extent, on the duration and severity of the original disease to which the pericardial suppuration is secondary. If my three cases are added to the ninety-nine cases mentioned in Pool's report, in which the patients were operated on for suppurative pericarditis, there have been forty-seven deaths and fifty-five recoveries. Some of the patients who recovered have shown a crippled condition of the heart due to intrapericardial or mediastinopericardial adhesions. The degree of myocardial degeneration also has a most important bearing on the ultimate prognosis in these cases.

I resected the fifth costal cartilage in my first case, in my second case, the sixth costal cartilage, and in my third case, the sixth and seventh costal cartilages. If I have another case, I shall make a hockey-stick incision, beginning at the fifth cartilage and progressing down along the left edge of the sternum and along the seventh cartilage, then I shall resect all three of these cartilages. This is the method proposed by Pool, and it impresses me as the best yet suggested. I believe that a local anesthetic is the anesthetic of choice, but if for any reason a general anesthetic is demanded, my preference would be for ethylene gas. Removal of the pericardial pus by suction rather than by irrigation at the time of operation, seems to be a step in the right direction. Postural treatment to secure drainage is also an important measure. There should not be any fixed rules about irrigation of the pericardium or about the placing of drainage material in the sac. Each patient should be treated according to individual indications.

#### ABSTRACT OF DISCUSSION

DR WYMAN WHITEMORE, Boston. The subject of pericarditis is of great interest to all thoracic surgeons. One great trouble is that few men treat many of these patients. In fact, I do not know of any one who has had any considerable number of these patients. There are certain points that interest me. The first is the diagnosis. As Dr Peterson has said, the diagnosis is often missed, this was particularly true before the roentgen ray was used. I think that now physicians and thoracic surgeons probably use the roentgen ray often and early in these cases, and that the diagnosis is not missed as frequently as it used to be. The second point is, as Dr Peterson has said, that this condition is always secondary to an infection elsewhere.

The third point that has always interested me, is the luck that the patient and surgeon have in these cases. By that I mean, suppose that a patient has pneumonia and a small empyema, which is drained, pneumococcic pericarditis develops. This patient has as good a chance to get well as the patient who has a streptococcic septicemia and develops streptococcic pericarditis. An operation in a case of streptococcic pericarditis does not offer the patient any hope of recovery.

I have had four cases. One was a pneumococcic case in which the patient recovered, this patient had an empyema and then a pericarditis, which was



interest that in seventeen of these cases the diagnosis of hernia of the cardiac end of the stomach through the esophageal opening was made by means of the roentgen ray. This is the most common type of hernia that occurs in adults, as it is shown in the cases reported.

In twenty-seven cases, herniation of the abdominal viscera into the thorax was the cause of the complaint, and operation was performed.



Fig 2—Diaphragmatic hernia with almost half of the stomach above the diaphragm through esophageal opening

Seventeen of the patients were males, and ten were females. The youngest patient was 5 years and the oldest 72 years. The age incidence in decades was from 1 to 10 in two cases, from 11 to 20 in three, from 21 to 30 in four, from 31 to 40 in three, from 41 to 50 in six, from 51 to 60 in eight, from 61 to 70 in none and from 71 to 80 in one.

into direct contact with the pericardium at this point by fluid lying behind the heart. Aspirations in the fifth left interspace just inside the left border of dulness should therefore follow a negative aspiration. At the sternal margin, I should regard the latter point the preferable one in all cases if it were not for the possibility of pleural contaminations in case the fluid is infected and the pleura not adherent.

In a few cases, in which I have failed to find fluid elsewhere, I have obtained it by aspiration in the fifth interspace at the right sternal margin.

There is no doubt that nearly all cases of pericardial effusion are secondary to infection elsewhere. I have had one patient with sterile tuberculous effusion from whom, however, 2 liters of pus were obtained. When the case came to necropsy, a few months later, examination failed to reveal any trace of primary infection, even in the glands. I reported this case as one of primary tuberculous pericarditis.

Even though the condition is secondary and the mortality high I believe that we should make every effort to establish the diagnosis early and to drain for all infected effusion. I am much interested in Dr. Peterson's method of drainage, but I have been so impressed by the value of a surgical solution of chlorinated soda in cases of empyema that I prefer to take my chances with the suction and irrigation drainage that its use involves. I had one patient with double streptococcic empyema and purulent pericarditis who apparently would have recovered following simultaneous irrigation of all cavities had he not died of a sudden hemorrhage into the pleural cavity on the tenth day.

DR. WILLI MEYER, New York. Since we have the roentgen ray, the enlargement of the heart's shadow is clearly seen, and there is also the possibility of finding it by percussion. We will thus be enabled to establish the diagnosis without much difficulty. No doubt these patients with a larger effusion in the pericardium suffer a great deal, and if there is even a suggestion of an effusion, it is an easy matter to ascertain whether this is present.

I thoroughly agree with what Dr. Hedblom said and also with the previous speaker. I would always favor aspiration in the fourth or fifth interspace close to the left side of the sternum, where one can be sure not to injure the internal mammary artery with the needle. If the needle usually is directed slightly upward and outward, it will be possible to strike the effusion in the majority of cases.

In 1908, I operated on a tuberculous patient with chronic pericarditis. He had been in the medical division of the Lenox Hill Hospital quite awhile and suffered intensely. Aspiration was performed by the method I have just mentioned, a bloody effusion was found—a dark fluid, which showed the decomposition of blood under the microscope. It came out easily in large amounts. An operation was performed and more than 2 quarts of fluid were found in the sac. Many of you have read the article on chronic pericarditis in 1904 or 1905, published by the late Professor Curschmann of Leipzig. He cited cases in which more than 3 quarts of fluid had been removed from the sac. That is easy to understand if one remembers that the pericardium touches the esophagus posteriorly. If a person has a large chest this mediastinal sagittal diameter is long, and so frequently the greater part of the fluid is behind the heart, so that the aspiration or evacuation of more than 2 or 3 quarts of fluid from the pericardium is possible and easily explained.

In our case aspiration was done first, then the fluid reaccumulated. After this, we decided to operate. I have not had time to look up the histories in my old cases, so I will not give you the details but only say that a large

diagnosed clinically as ulcer or disease of the gallbladder. The most common symptoms noted by Giffin were (1) pain in the epigastrium and chest immediately after eating, (2) paroxysms of smothering without apparent cause and (3) vomiting without premonition. Healy<sup>13</sup> gives as the principal symptoms (1) substernal pain, (2) vague gastric



Fig 4—Traumatic diaphragmatic hernia following gunshot wound. A bullet may be seen in left flank at the level of the eleventh rib. Almost the entire stomach is in left thoracic cavity.

distress and (3) vomiting in the morning without hyperacidity. The cardinal symptoms given by Oden<sup>14</sup> are (1) epigastric pain immediately

13 Healy, T. R. Symptoms Observed in Fifty-three Cases of Nontraumatic Diaphragmatic Hernia, *Am J Roentgenol* **13** 266, 1925.

14 Oden, R. J. E. Diaphragmatic Hernia, *Ann Surg* **78** 660, 1923.

would put my fingers into the pericardium, as I do in the pleural cavity, make a puncture farther outside with the knife, introduce the tube for air-tight drainage into the sac, under the guidance of eyes and fingers, and close the original incision. Then I would have the combination of open incision and air-tight drainage, if the various tissues, muscles, fascia and skin are carefully sutured just over the entrance of the tube into the pericardium and the drainage tube properly secured, the method will be the same as the one that has been tested successfully in air-tight drainage of the pleura in cases of empyema.

DR FREDERICK T LORD, Boston. I should like to call attention to certain aspects of the diagnosis in these cases. The infrequency of pain as a symptom of inflammation of the pericardium has long been recognized and has until recently not been satisfactorily explained. Capps of Chicago has shown by experimental mechanical irritation that the interior of the pericardium is insensitive at all accessible points except in the region of the left inferior aspects of the sac. He ascribes the sensitiveness of this part to irritation of branches of the phrenic nerve. Judging by these experiments, the infrequency of pain in the presence of pericarditis may be attributed to absence of a sense of pain over the greater part of the pericardium. Absence of pain should not be taken as an indication of absence of pericarditis.

In the discussion, reference has been made to the presence of posterior accumulations of pericardial fluid, and this is another source of error in the diagnosis. When the heart becomes adherent to the anterior part of the pericardial sac, fluid may accumulate for the most part posteriorly and compress the lung in this region. The most significant physical signs of pericardial effusion may then be found in the left side of the back, and it is common in such cases to be able to demonstrate in the region of the left scapula an area of dulness with bronchial breathing, egophony and increase in the speaking and whispering voice and diminished tactile fremitus.

Roentgen-ray examination also furnishes important evidence of pericarditis with effusion. The shadow of the heart is triangular, and the sides of the triangle are straighter than normal as a result of obliteration of the indentation on each side at the junction of the auricles with the mediastinum, and on the left at the junction of the auricle with the ventricle.

DR N W GREEN, New York. The discussion and the reports of Dr Peterson's cases have been stimulating and impressive. I have had limited experience with cases of effusion of the pericardium, but the discussion Dr Whittemore brought one or two points to my mind, one of which was that when a patient has a streptococcal infection of the blood, the physician considers the case hopeless. A streptococcal infection of the blood predicates a blood-borne infection, and it seems to me that one should look for infection of the accessory sinuses, which in cases of diseases of the ear are often followed by pneumonia and sometimes by *Streptococcus hemolyticus* infection of the blood. I believe that it would be a good plan to determine whether there is any thrombosis or lateral thrombus in the jugular vein. If one could get rid of the primary source of the infection of the blood stream I do not think that *Streptococcus hemolyticus* infection of the blood would necessarily indicate a fatal outcome. I have had experience in one case of that kind, and the course of the disease was very much as I have outlined, first an infection of the ear, then of the mastoid, then in the jugular vein and then pneumonia. The patient did not have pericarditis, but a *Streptococcus hemolyticus* infection of the blood.

The inconstancy of these symptoms is undoubtedly produced by the varying site of the hernial opening and the difference in the degree of functional adjustment of the thoracic and abdominal viscera. It is evident that diagnosis by means of the history alone may be difficult,

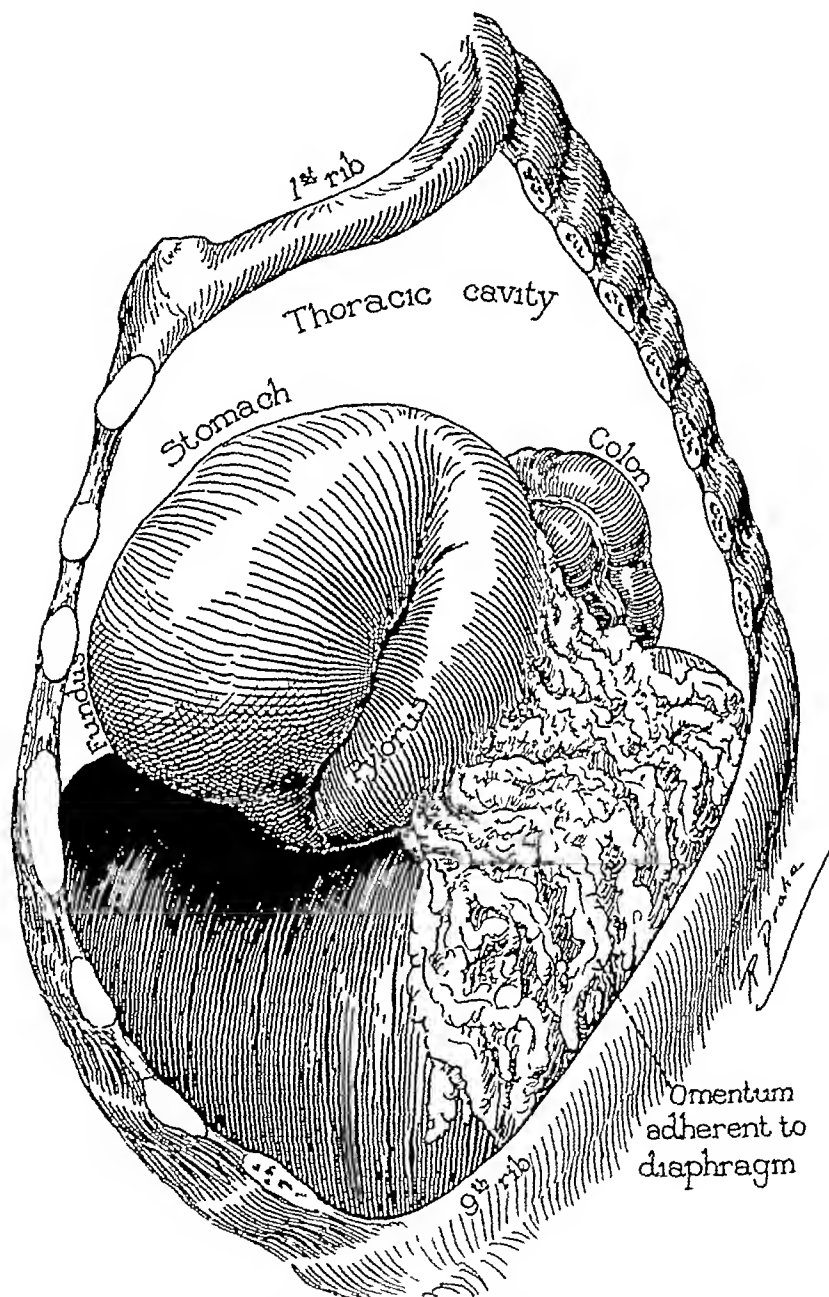


Fig 6—Left diaphragmatic hernia. Almost the entire stomach and a portion of the colon are in the left thoracic cavity. The omentum is adherent to the diaphragm and the under surface of lung.

however, such diagnosis is important and when possible, will obviate useless treatment. Because of the vague symptoms simulating some thoracic or abdominal disease, of which disease of the gallbladder and of the stomach are most common, operation may be advised. Diaphragmatic

could not be stopped. The cause of this bleeding remained obscure, although autopsy was performed. The only thing the pathologist suggested was that the motion, the friction between the heart and the pericardium, both being granulating surfaces, had the effect of continuously brushing off the apexes of the granulations. It seemed unusual. I had never seen it described and had never heard any one speak of it. The patient was not given a transfusion of blood. This was a long time ago. Clinically, the condition resembled hemophilia, it may be, however, that this resulted from some alteration in the blood brought about by scarlet fever.

The second patient had a large suppurating pericardial sac which was opened under local anesthesia and drained with protective tissue. The sac was irrigated daily. The sac became clean, but the pus accumulated rapidly behind the heart. A little later, the patient was treated by the instillation of mercurochrome-220 soluble, and the interesting fact was that in two or three hours after a dressing, when we had cleaned the pericardial sac the patient began to have a free discharge of pus. At autopsy, an apical tuberculous cavity was found with a sinus running from it to the suppurating pericardial sac, we had been dealing with a secondary type of pericarditis and of a variety I have never seen described.

DR DEW ANDRUS, Cincinnati. I want to say only a word about two cases we have had in Cincinnati. One of these patients had an abscess in the posterior portion of the pericardium. He was an Italian ex-soldier and had been shot in the back of the neck, a piece of tunic becoming embedded in the tissues. Before he came to us, he had had an abscess on the right side of the neck which was healed at the time of admission. Following a stay in the hospital for tuberculosis, he was brought to the general hospital with the diagnosis of abscess of the lung posterior to the heart. Dr Heuer approached it from the side in the posterior axillary line, and to his surprise found that it was not in the lung, but in the pericardium. The nature of the infection was not definitely determined. Subsequently, the patient developed an abscess in the groin, and after repeated roentgenograms, we discovered a collapsing lesion of the upper lumbar vertebra. Drainage of a lumbar abscess yielded the typical sulphur granules and ray fungi.

The other case was that of a boy, about 18, who was stabbed over the sternum with a knife. His wound was closed before he came to the hospital. Subsequently he developed shortness of breath, etc., which pointed to a mediastinitis. A roentgenogram revealed  $1\frac{1}{2}$  inches (3.77 cm) of knife blade broken off and buried in the sternum. Dr Heuer resected a portion of the sternum and costal cartilages, removing the knife blade, and found a suppurative pericarditis. The boy pursued a course similar to Dr Miller's patient having repeated small hemorrhages from the pericardium, which we felt were due to grating of the granulations with the pulsations of the heart. Despite repeated transfusions, the patient subsequently succumbed to severe secondary hemorrhage.

In the children who come in with coincident empyema, pneumonia and pericardial effusion, we have found it useful to increase the margin of safety. Decrease the load on the heart by giving these patients oxygen intranasally. Sometimes, even when they are not cyanotic, the administration of oxygen will make the breathing easier and reduce the load on the heart.

DR HUGH AUCHINCLOSS, New York. Dr Peterson's cases are noteworthy and most encouraging. Our experience with suppurative pericarditis at the Presbyterian Hospital has been chiefly with adults. The first patient who recovered was a child, the case was reported a number of years ago by

hernia may be discovered by exploration of the diaphragm during an operation for some other condition, particularly an upper abdominal operation, if disease of the gallbladder or stomach is suspected but not found. During the last year one esophageal hernia was found during an operation in a case with an indefinite history of cholecystitis in which the stomach had not been examined roentgenologically prior to operation.



Fig 8—Diaphragmatic hernia with about one third of stomach herniating through the esophageal opening, large perforating gastric ulcer high on the lesser curvature of the stomach

#### TREATMENT

The treatment in cases of diaphragmatic hernia in which the symptoms are mild and there is no obstruction, may be medical. Many patients go through life without sufficient symptoms to warrant operative intervention. In chronic cases with attacks of incarceration or obstruction

for drainage. Drainage through the anterior wall of the chest is easy to perform under an anesthetic. The closed system of drainage could be established with the pericardial sac draining into the pleural sac and then out. The anterior drainage could then be established at any time under local anesthesia. Drainage along the straight sinus is another problem. Accumulations have been seen on the other side of the heart. It seemed in the last case I had that accumulations of pus were found in the place at which the pocketing appeared as well as behind the heart. In my case in which the method of open drainage was employed, we used a surgical solution of chlorinated soda (Dakin solution), and placed the finger under the heart and a catheter straight around it, so that the catheter came up around the upper margin. It was possible to keep that part clean by drainage suction.

DR. PETERSON. The diagnosis in these cases of suppurative pericarditis is not as simple as is generally supposed. The roentgenologist if I recall correctly, made the diagnosis in all three of my cases. The roentgenogram is the most valuable aid in settling the question of diagnosis.

I feel that Dr. Hedblom's case of "primary" pericarditis is open to question. I merely suggest that it might have been one of tuberculous origin, as I cannot conceive of any case being primary.

I feel that the prognosis, as I said in my paper, depends largely on the duration and severity of the original infection to which the pericarditis is secondary. The mortality rate will be relatively higher in infants than in older subjects, just as it is in the empyema of infancy.

I want to thank Dr. Lilienthal for answering the question about closed drainage of the pericardium. I do not see that one can liken the drainage of the pericardium with drainage of the pleural cavity. Not only is the physiology different but the physics to be considered in the former is also different. I cannot see any great advantage in the closed method advocated by Dr. Whittemore and approved by Dr. Meyer. I feel, however, that postural drainage is a step in the right direction.



were employed, the type depending to some extent on the site of the opening in the diaphragm, as far as could be determined by roentgenologic examination. If the opening was anterior, the abdominal approach was used, and if posterior, the thoracic approach.

Nineteen of these cases have previously been reported by Giffin, Balfour<sup>16</sup> and Hedblom,<sup>17</sup> who made a complete review of the cases in which operation was performed up to 1925, I shall not include these cases in this report.

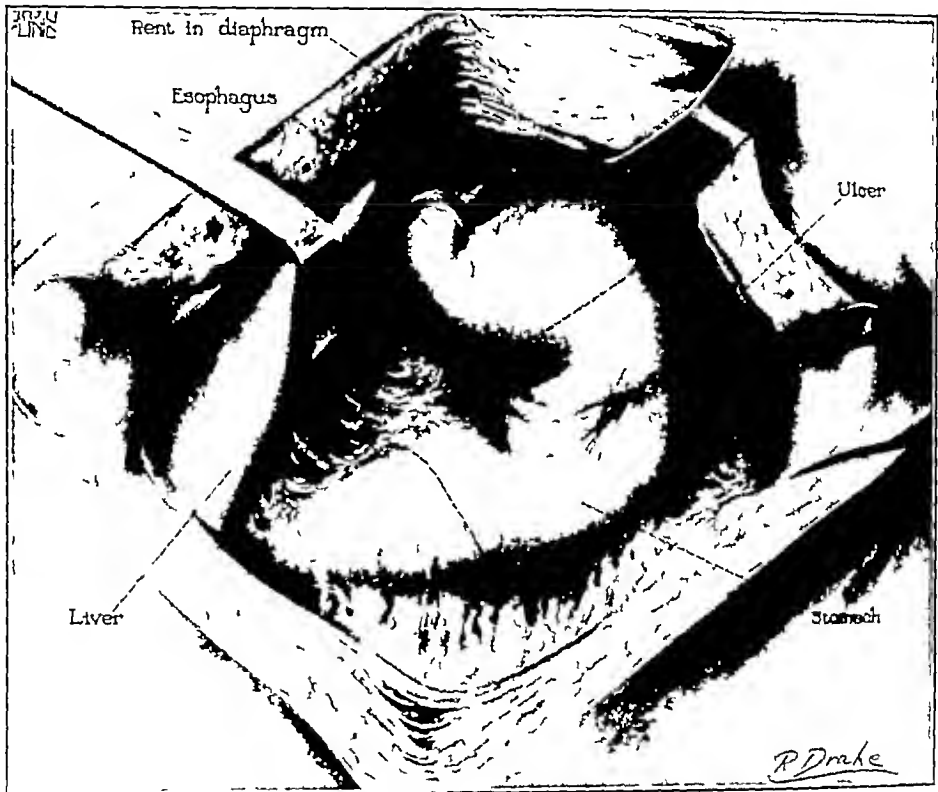


Fig 10—Exposure of cardiac end of stomach after reduction from hernial sac. A large perforating gastric ulcer is shown high on the lesser curvature of the stomach, about 7.5 cm. from the cardia and a large hernial opening just above and to the left of the esophagus. The dotted lines outline the area of gastric resection.

In the last two years eight patients have been treated surgically. In five of these there was no history of injury. In three cases operation had been performed previously for the same complaint.

16 Balfour, D. C. Nonstrangulated Diaphragmatic Hernia due to Indirect Injury, *Ann Surg* 63:78, 1916.

17 Hedblom, C. A. Diaphragmatic Hernia, A Study of Three Hundred and Seventy-eight Cases in Which Operation was Performed, *J A M A* 85:947 (Sept 26) 1925.

The systolic blood pressure was 150, diastolic, 85 Dilated veins were not seen on the thorax, and cyanosis was not present

Operation was performed under local infiltration anesthesia with procaine hydrochloride A collar incision was made and a lipoma about twice the size of a hen's egg was found lying beneath the sternothyroid and the sternocleidomastoid muscles It lay next to the right lobe of the thyroid gland, which seemed normal, and it extended downward into the anterior mediastinum for a distance of about 4 cm It was removed without difficulty by pulling it upward in much the same manner in which a substernal thyroid is removed The only muscle cut was the platysma Closure was made without drainage. Within a few hours after the operation the hoarseness had disappeared, and the patient stated that the dyspnea was not present He was discharged one week after the operation Six weeks later he was seen again following an attack of acute cholecystitis Hoarseness or dyspnea had not been present since the discharge He would not consent to an operation on the gallbladder

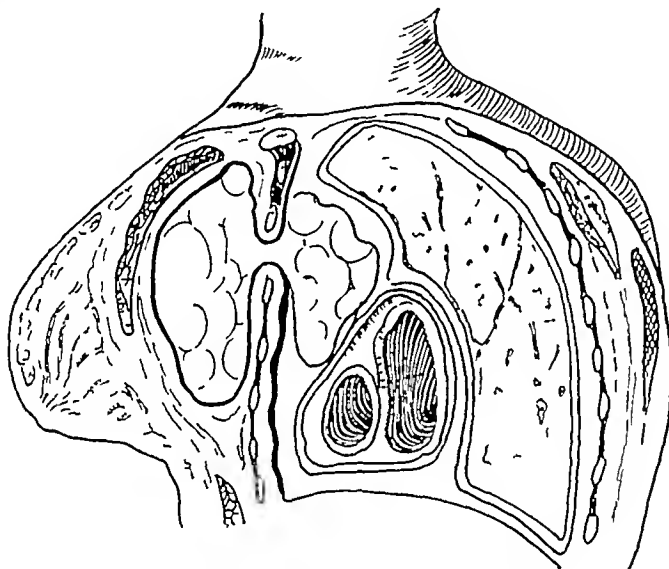


Fig 1—Diagram in Gussenbauer's case

After removal, the tumor was found to measure 9 by 5 cm On microscopic examination, it proved to be a simple lipoma

This case, therefore, was one of lipoma of the anterior mediastinum which caused sufficient pressure to produce hoarseness, dyspnea, cyanosis and possibly a partial paralysis of the right leaf of the diaphragm by involvement of the right phrenic nerve

The few instances of lipoma of the mediastinum which we could find recorded in the literature show only two other cases besides our own in which an operative removal was carried out successfully This is probably to be explained by the fact that most of the other cases occurred during the early days of antiseptic surgery In some of the reported cases, the tumor was limited to the mediastinum, in some it occupied the pleural cavity also, while in others it was located both subcutaneously and in the anterior mediastinum In all only nine cases

In one case the gallbladder was removed for gallstones at the time of repair of the hernia, and in one case the pyloric four fifths of the stomach was resected for a large perforating ulcer high on the lesser curvature of the stomach. These lesions were undoubtedly partly responsible for the symptoms (figs 8, 9, 10, 11, 12 and 13)

I prefer the abdominal approach in most cases. The herniated abdominal viscera can be brought under direct observation, and any injury that may be present in traumatic cases can be more readily

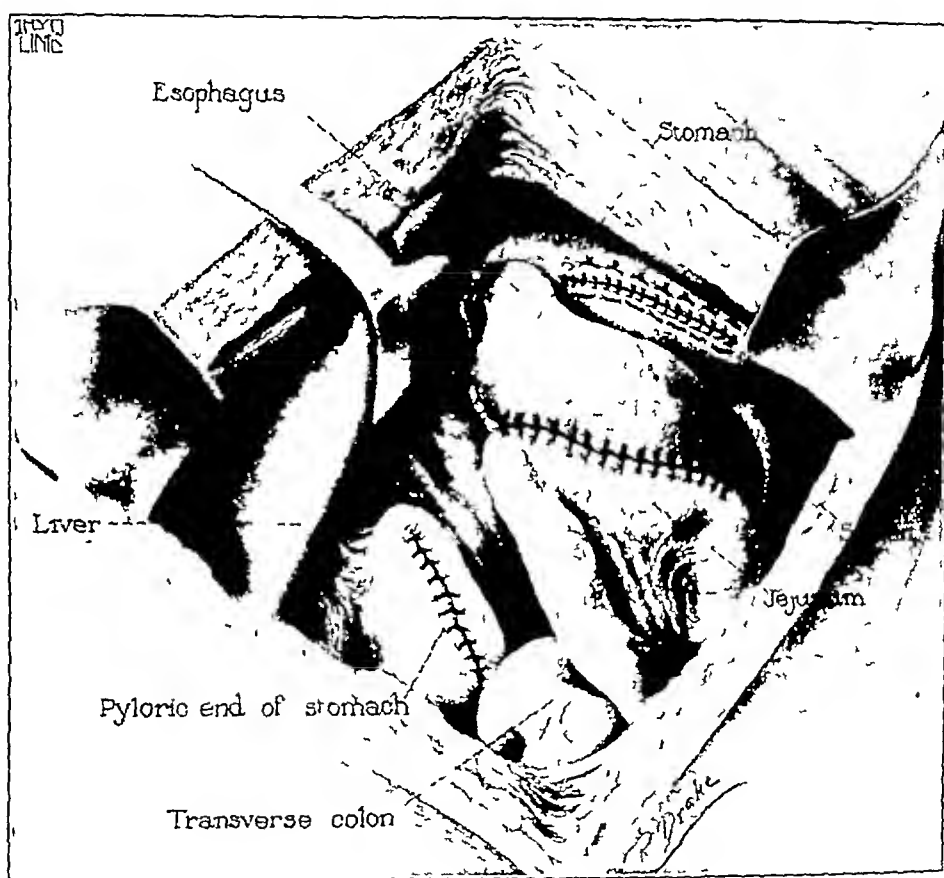


Fig 12—Closure of hernia opening in diaphragm with interrupted linen catgut sutures, resection of four fifths of the stomach, anticolic anastomosis of cardiac end of the stomach to the jejunum with closure of pyloric end of the stomach

repaired. There is no danger of injury to abdominal viscera during closure of the hernia. There is less deformity following operation, and the risk of the operation and the chance of postoperative complications are probably less. The abdominal approach permits exploration of the abdomen for other associated lesions which may be the cause of part of the symptoms. These lesions may be surgically treated at the same time if it is thought advisable. If the patient's condition does not permit

including our own, have been reported. Probably the condition is much more frequent than this small number of cases would indicate. There are several instances of intrapleural lipoma developing apparently from the subpleural fat, but they are not included in this report. The case described by Czerny<sup>1</sup> is an example of this.

In his classic treatise on pathologic anatomy in 1856, Cruveilhier stated that during an operation for the removal of a lipoma on the

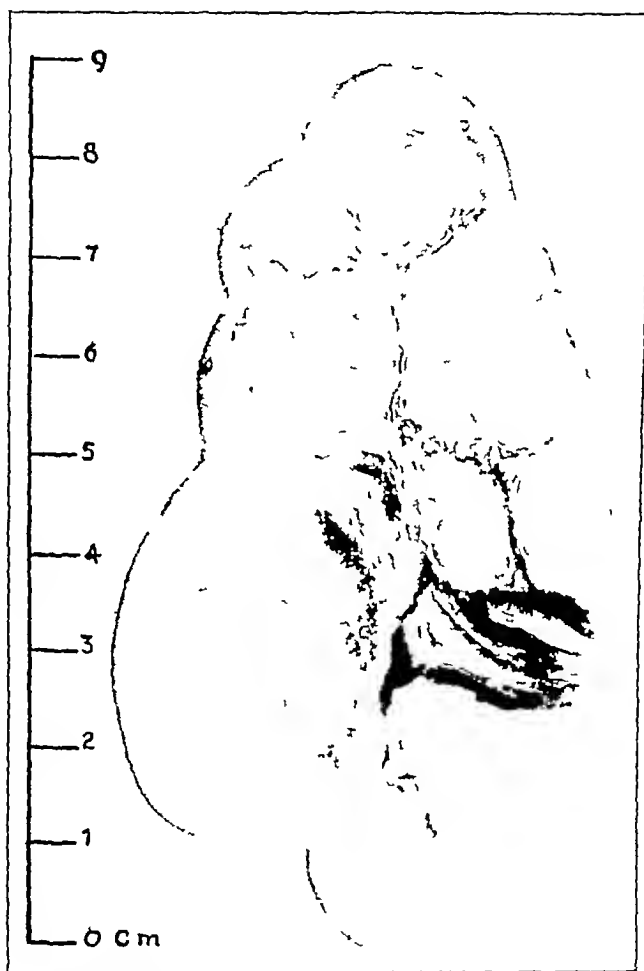


Fig 4—Appearance of specimen after removal in author's case

front of the sternum, several prolongations were observed to continue into the anterior mediastinum. Most of these were withdrawn and cut off. The patient died of suppuration of the anterior mediastinum. Cruveilhier also mentioned that Morel-Lavallée removed the superficial portion of a lipoma, which continued into the anterior mediastinum, from the sternal region. The mediastinal portion was not disturbed.

<sup>1</sup> Czerny. Exstirpation eines kopfgrossen subpleuralen lipoms. *Wien med Wchnschr* 25 156, 1875.

combined method I have not found this necessary, but undoubtedly there are cases in which a satisfactory result cannot be secured in any other way

Gastric lavage should always be carried out just before operation and the tube left in the stomach or inserted after the abdomen is opened. This not only relieves the stomach of gas and thus aids in the reduction of the hernia, but also helps to determine the position of the cardia, this may be helpful in cases of esophageal hernia with adhesions and permits more accurate closure of the opening.

In seven of the cases the hernial opening was closed with chromic catgut reenforced with linen sutures. In one case the defect in the diaphragm was so extensive that closure was impossible, and the stomach was sutured to the abdominal wall.

There were no deaths, and convalescence was uneventful in all cases, except for minor complaints. The results, as shown by replies to recent questionnaires, are satisfactory, but some are too recent to be considered final. The most recent operation was performed three and one-half months before this paper was written. Four patients say that their symptoms have been completely relieved. The hernia was of traumatic origin in three of these. The fourth patient did not give a history of injury, and gastric resection for ulcer high on the lesser curvature of the stomach was performed as well. Two patients continue to have moderate gastric symptoms without evidence of recurrence four months and six months, respectively, after operation. In the case in which part of the diaphragm was absent and the stomach was sutured to the abdominal wall, relief has been only partial. In one case the hernia and symptoms recurred two months after the operation.

#### SUMMARY

The embryonic formation of the diaphragm predisposes to herniation at certain sites.

The symptoms of diaphragmatic hernia are varied, and clinical diagnosis is difficult without the aid of roentgenologic examination. Obscure upper abdominal symptoms demand roentgenologic examination of the diaphragm. Roentgenologic examination is often helpful in determining the site of the hernial opening. When the diaphragmatic hernia produces mild symptoms without incarceration of viscera, the patient may be kept under observation and medical management, but progression of symptoms calls for operation. Definite attacks of obstruction due to incarceration or strangulation of abdominal viscera demand operation.

The operative approach may be thoracic, abdominal or combined abdominal-thoracic, but the abdominal is usually preferable or the com-

case of a boy, aged 22 months, from whom he successfully removed a lipoma of the anterior mediastinum. There was a painless swelling in the front of the chest, which had grown steadily. The tumor was overlying the fifth, sixth and seventh costal cartilages. It had a lobulated surface and was adherent to the adjacent tissues but not to the skin. At operation an incision was made parallel to the sixth rib, and a fatty mass was found passing through the sixth intercostal space into the thoracic cavity. The sixth and seventh costal cartilages were resected, and a circumscribed fatty tumor was easily removed. Recovery was excellent. Microscopic examination of the mass showed it to be a simple lipoma. In 1925, Lemon<sup>6</sup> reported the case of a man, aged 46, who had dyspnea, swelling of the neck, cough, loss of weight, tumor in the left supraclavicular fossa, dullness over the upper sternum and distant breath sounds over the chest. Two biopsies were performed, the first of which was said to show an osteochondrolipoma and the second a lipoma. The patient weighed 221 pounds (100.2 Kg). The veins in the upper part of the body became dilated. Vertigo, somnolence, dyspnea, cyanosis and edema developed, and the patient became gradually worse. At autopsy a lipoma of the anterior mediastinum was found which was adherent to the trachea, aorta and right lung.

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6 Lemon, W. S. Lipoma of Mediastinum, *M. Clin. N. Amer.* 8:1247, 1926.

but covered by the liver anteriorly, was a large opening, a congenital defect of the diaphragm, through which portions of the gastro-intestinal tract had slipped into the thoracic cavity. In pulling further, we could slowly get a good portion of the intestines into the abdomen, but at the same moment some fecal matter escaped. I was extremely sorry that I had decided to start the operative procedure by way of the abdomen. With such a large portion of intestines in the thoracic cavity, the lung had to be compressed materially on that side for a long time. With 1 mm of oxygen pressure, one could have overcome any difficulty so far as a large opening in the chest was concerned. I should have made an intercostal incision and determined the condition. I could have seen it easily because a constriction of the middle of the transverse colon was causing the trouble. There was a clear local gangrene at this place. The primary intercostal incision would have been the better surgical procedure. After I had seen that there was a suppurative condition, I could have worked from above and below.

I have drawn a number of lessons from that case in addition to realizing the necessity for gastric lavage. I would never advise starting with an abdominal incision in a complicated case of diaphragmatic hernia. There is no harm in performing an exploratory thoracotomy. Had I have done so, I would have found the gangrene of the intestine and the hernial aperture at once, which was utterly impossible by way of the abdomen, because the right lobe of the liver was lying in front of it.

From a technical point of view, I would say as in so many other cases, that one must consider the individual case, as was emphasized in a number of other thoracic diseases.

Dr Harrington's eight cases make a wonderful series for one man to observe in such a comparatively short time, but he is working at the Mayo Clinic with its unlimited material. All his patients were operated on by way of the abdomen, and every patient has recovered, which speaks for itself. Yet I would say again, let us consider each case by itself, and when there seems to be a great deal of complication let us start the operative procedure by way of the thorax. Personally, I would then add an abdominal incision, so that I could see how I could replace the abdominal organs and secure them with sutures before the hole in the diaphragm was closed.

DR TRUESDALE, Fall River, Mass. Dr Harrington has demonstrated in a picturesque and practical manner those developmental deficiencies in the diaphragm that may be conducive to the occurrence of hernia. He has shown, too, that the stomach is more often involved in cases of hernia than any other of the abdominal viscera. When the stomach passes through the opening in the diaphragm, it can pass back and forth, and unless it is markedly constricted, it can be relieved. If a portion of the stomach has passed through the diaphragm and it becomes constricted, a stomach tube cannot be placed in that portion of the diaphragm which is above the constriction.

The stomach never becomes strangulated, because there is great elasticity to the hernia ring. When it fills with gas the pressure expels the contents below the diaphragm and thus empties. To prepare the patient for operation by washing out the stomach, as Dr Harrington describes, is the best policy, without a question. It is seldom if ever necessary to operate for hernia of the stomach, as an emergency measure.

On the other hand, that type of case which involves the small intestines and the transverse colon, which, as the statistics of Dr Harrington and Dr Hedblom have shown, is nearly 50 per cent of all cases, often presents the picture of acute obstruction.

Rowlands <sup>4</sup> found records of two cases in Guy's Hospital, London, from 1856 to 1920. Cruickshank <sup>5</sup> discovered two cases in a series of between 1,700 and 1,800 necropsy examinations, Rendich <sup>6</sup> reported two cases out of 5,033 clinical examinations at Bellevue Hospital, New York, Macmillan <sup>7</sup> found but three cases in 15,000 roentgenologic examinations at United States Army General Hospital No. 1, Beclere, <sup>8</sup> in 5,000 roentgen-ray examinations, found two cases, Morrison <sup>9</sup> reported forty-two cases of 3,500 gastric cases studied, and Carman, <sup>10</sup> in 1924, gave the ratio in the Mayo Clinic of 1 : 18,000.

#### ANATOMY

The diaphragm is a single independent dome-shaped muscle arising from the circumference of the lower part of the thorax and when normally formed completely separates the abdominal and thoracic cavities. The muscular structure of the diaphragm in the adult person is divided into three portions according to their origins, the sternal, the costal and the lumbar. The sternal is the weakest of these portions and the lumbar the strongest. All three portions are inserted into the margin of the central tendon. The sternal portion consists of a few slender fasciculi arising from the posterior surface of the xiphoid cartilage. There are muscular deficiencies on each side of the cartilage filled with areolar tissue and covered with pleura and peritoneum through which the superior deep epigastric vessels pass. These deficiencies are called the foramina of Morgagni or Larys' spaces. The costal portion forms the main part of the dome of the diaphragm and arises by broad bands of muscle from the lower six costal cartilages and from the eleventh and twelfth ribs, interdigitating with the transversalis muscles. This portion covers the greatest area. There are often areas devoid of muscle tissue between the individual bands that arise from the wall of the chest. The lumbar portion arises from the

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4 Rowlands, E. R. B. A Case of Diaphragmatic Hernia, *Guy's Hosp. Gaz.* **34** 426, 1920, Diaphragmatic Hernia, *Guy's Hosp. Rep.* **71** 91, 1921.

5 Cruickshank, J. N. Two Cases of Congenital Diaphragmatic Hernia, *Glasgow M. J.* **105** 81, 1926.

6 Rendich, R. A. The Radiographic Examination of the Alimentary Tract with Analysis of Routine Examinations of 5,033 Hospital Cases, *J. Radiol.* **5** 124, 1924.

7 Macmillan, A. S. Diaphragmatic Hernia, *Am. J. Roentgenol.* **7** 143, 1920.

8 Beclere, quoted by Morrison. Diaphragmatic Hernia of Fundus of Stomach through the Esophageal Hiatus, *J. A. M. A.* **84** 161 (Jan. 17) 1925.

9 Morrison, L. B. Diaphragmatic Hernia of Fundus of Stomach Through the Esophageal Hiatus, *J. A. M. A.* **84** 161 (Jan. 17) 1925.

10 Carman, R. D., and Fineman, Solomon. The Roentgenologic Diagnosis of Diaphragmatic Hernia, with a Report of Seventeen Cases, *Radiology* **3** 26, 1924.



difficulty in reducing the hernia. The bowel and omentum were tied around the opening on the under side, and I could not remove the adhesions without injuring the intestines, so I continued the incision downward, opened the peritoneal cavity and operated from below and above, cut the diaphragm out from the hernial opening toward the periphery, reduced the bowel and omentum and sewed up the enlarged opening in the diaphragm. That operation was performed first by Berard in France. His patient succumbed, undoubtedly because Berard was obliged to operate during a period of acute intestinal obstruction. Then another French surgeon, Anvray, repeated the operation on a patient with intestinal obstruction who had come to him reasonably early. He succeeded in reducing the hernia, and his patient recovered.

Dr Stone of Baltimore had a similar case, in which he made first an abdominal incision and then an incision through the wall of the chest.

The extension of the lapel incision is simple. It just crosses the diaphragm, so that one does not need to open the abdominal cavity any more than from 1 to 2 inches (2.5 to 5 cm) in order to have access to the adhesions on the under side. Dr Stone's patient recovered. His difficulty was above the diaphragm, and it seems to me that in those cases the thoracic incision gives more ready access to the diaphragm and will serve a purpose which cannot be obtained by the peritoneal route alone.

DR L. T. LEWALD. I should like to call attention to two conditions in which an operation should not be performed unless some complication has occurred. I refer particularly to complete absence of the left half of the diaphragm. Dr Harrington referred to that under his heading "partial absence." The other condition is that which occurred in a case referred to by Dr Meyer, the disease was thoracic stomach, in which there is no deficiency in the diaphragm, but the stomach is developed above the diaphragm. Dr Harrington spoke of the development of the diaphragm just at the time that the stomach was also developing, and it is now possible to conceive of the stomach as being developed above a perfectly developed diaphragm. Percival Bailey first called attention to this in the dissecting room. I have reported two cases of this sort,<sup>18</sup> and another case has been recently reported in Liverpool by Roberts.<sup>19</sup> In one of my cases the roentgenograms determined the exact position of the diaphragm in relation to the stomach and the stomach was above the intact diaphragm. An operation was performed because the child had twenty-four hour retention in the stomach because of pyloric obstruction. He was undersized, and at the age of 7 he was smaller than a boy of 4. Dr Downes performed a gastro-enterostomy.

The other problem is to determine roentgenographically whether there is need for operation in a case of complete absence of half of the diaphragm, and then to operate only on such patients as show some complication.

I should like to ask Dr Harrington if he can explain how this complete absence of half of the diaphragm occurs.

I have two patients of this type. In one case, we feel we have been able to demonstrate the fact that the diaphragm is absent completely by comparing it with a normal side view. There is no evidence of a diaphragm on the left side. In the other case intestinal contents in the chest cavity, the stomach down in the pelvis and only one leaf of the diaphragm are demonstrated.

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18 LeWald, L. T. Congenital Absence of Left Half of Diaphragm, *Arch Surg* **14** 332 (Jan) 1927.

19 Roberts, R. E. *Brit J & Radiol* **32** 11 (Jan) 1927.

portion of the diaphragm arises chiefly from the inner lumbocostal arch with only a few fibers arising from the external lumbocostal arch. There is usually a triangular space of muscular deficiency between the outer crus of the lumbar portion of the diaphragm, the last muscular part of the costal portion of the diaphragm and the twelfth rib. The apex of the triangle is curved upward and forward toward the tendinous portion of the diaphragm. The base is turned downward and somewhat backward and partly rests on the twelfth rib, but sometimes it extends in front of the body of the psoas muscle. The borders of this hiatus are muscular and are more or less of sphincter-like construction. The space is closed by a membrane which consists of two sheaths, the upper sheath comes from the pleura, and the lower sheath is thin and is a continuation of the iliac fascia. This space was first described by Bochdalek, in 1848, and has been named the foramen Bochdalek.

The central tendon of the diaphragm is reniform, with the central portion slightly curved and extending into the dome, of which the greater portion is on the right side. At the base of this right portion and entirely within the tendon is a large quadrilateral foramen which gives passage to the inferior vena cava. This opening is on a level with the disk between the eighth and ninth dorsal vertebrae.

The diaphragm receives its innervation from the phrenic (usually from the fourth and sometimes through branches from the third and fifth cervical roots), the sympathetic and the intercostal nerves which send motor and sensory fibers to its peripheral parts (fig. 1).

#### EMBRYOLOGY

The formation of the diaphragm from embryonic structures is a highly complex process, as its muscular elements are derived from several sources.

The anterior, lateral and central parts, which comprise the greater portion of the diaphragm in the adult, are formed from the transverse septum and fused ventral mesentery. The remaining, posterolateral portion is formed by the fusion of the dorsal mesentery and the mesoderm derived from the receding wolffian body and the pleuroperitoneal membrane derived from the pulmonary ridge. It is difficult to determine the exact amount of the muscle tissue that is derived from each of these structures, as there is probably considerable variation, but it is also probable that the dorsal mesentery forms the posterior and central portions containing the esophageal opening. The mesodermic cells from the receding wolffian body form the right and left crura. The pleuroperitoneal membrane grows ventrally and closes the remaining opening (hiatus pleuroperitonealis) between the peritoneal celom and pleural celom, by fusing with the transverse septum, and forms the lateral portion of the diaphragm. Failure of fusion or proper deposition of the



Fig 14—The chest before the barium meal



Fig 15—The stomach immediately after the barium meal

In the foregoing it is seen that embryonic herniation would occur most commonly in the embryo from 11 to 20 mm. Congenital herniation of somewhat later formation can be explained on many of the same grounds. It is due to the failure of parts of the diaphragm to mature or to excessive degeneration of muscle elements in the formation of the central tendon.

#### CLASSIFICATION

Numerous classifications of diaphragmatic hernia are based on embryology, etiology, pathologic anatomy, the site of the opening in the diaphragm, the presence or absence of a sac, the contents of the hernia and other conditions. It is difficult or impossible to make most of these classifications clinically, they can usually be made only after operation or at necropsy. From a clinical and surgical standpoint, the history of injury is important in determining the type of treatment to be instituted and the probable prognosis in surgical cases. Better results are usually obtained from operation in cases of traumatic origin than in the cases due to embryonic defects. For this reason I have classified all types in two main groups, nontraumatic and traumatic, and subdivided these according to the various common types as follows:

##### I Nontraumatic

- 1 Congenital, due to embryonic deficiency, of which the most common sites in probable order of frequency of occurrence are (a) through the hiatus pleuroperitonealis (foramen of Bochdalek) without an enclosing sac, (b) through the dome of the diaphragm, (c) through the esophageal opening, (d) through the foramen Morgagni and (e) through the gap left by absence of the left half of the diaphragm.
- 2 Acquired after birth through an embryonic fusion point of the diaphragm, it may occur at sites named under congenital types.

##### II Traumatic

- 1 Indirect injury to diaphragm, it may occur at any point but usually through an embryonic fusion point, the result of crushing injuries and usually with a sac.
- 2 Direct injury to the diaphragm, the hernia may occur at any point and is usually the result of penetrating wounds (gunshot or knife wound) and usually without a sac.

#### MAYO CLINIC SERIES

Since 1908 fifty-one cases of diaphragmatic hernia have been diagnosed at the Mayo Clinic, of this number twenty-four were not considered surgical. In the latter the diagnosis was made by roentgen-ray examination during the course of the general examination, and it was not thought that the hernia was producing sufficient symptoms to warrant surgical intervention at that time. Many of the patients are under treatment for other conditions and return for observation from time to time, ultimately some of them will probably come to operation. It is of

this procedure could scarcely be imagined, the heart being under my fingers. After the heart had been massaged for about half a minute, its beat improved considerably, and within a minute it had returned to about as good a condition as it had been in before the emergency occurred.

The hernial opening was an enlargement of the esophageal hiatus in a direction to the left and slightly forward. It was large enough to admit three fingers. There was no hernial sac, merely an open window leading directly into the pleura. After the stomach had been emptied of its fluid with the aid of a stomach tube, the hernial opening was closed by four silk sutures, a



Fig. 17—Large bowel after barium clysma

procedure which was rendered somewhat difficult by the fact that the anterior border of the opening was partly concealed by the liver which had to be drawn forward to permit placing the suture. After the end of the operation some fluid was removed from the trachea and bronchi through the bronchoscope by Dr. Kernan. The patient did fairly well at first, but died on the following day.

The hernial ring in this case was not a separate opening but an extension of the esophageal hiatus. The esophagus came down through it in the normal way. The cardiac end of the stomach was in the abdomen, the rest of the stomach, about four fifths of it, being turned upward, formed a sharp kink.

The average duration of symptoms at the time of operation was nine and a half years, seventeen of these patients gave no evidence of injury, while ten dated the onset of their symptoms from severe injuries

### SYMPTOMS

The symptoms are dependent on the organs involved in the hernia. Lacher<sup>12</sup> states that every abdominal organ except the genitalia, bladder and rectum has been found in the thorax at least once. It is apparent that the symptoms will be varied and inconstant, in general they may be divided into thoracic symptoms, which are probably least noted, and abdominal symptoms, which are the most constant. The thoracic symptoms are caused by encroachment on the pleural space with impairment of respiration and circulation. The most common of these are dyspnea, cyanosis, palpitation of the heart and pain or sense of fulness

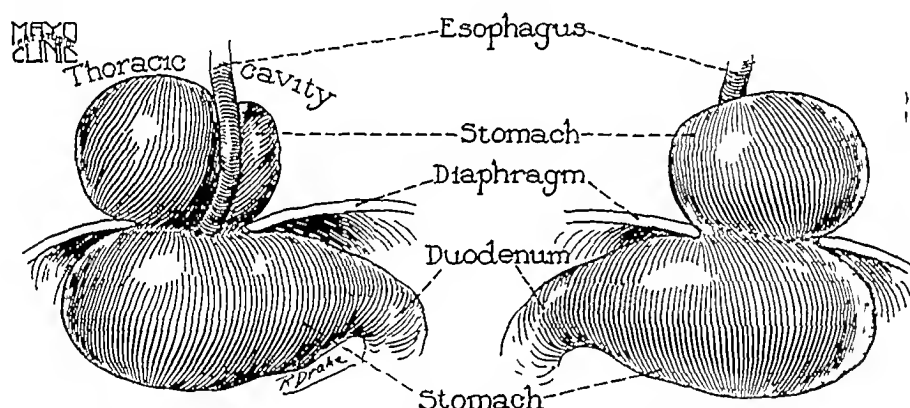


Fig 3—The portion of the herniated stomach posterior and to the right of the esophageal opening with pressure and partial obstruction to the lower portion of the esophagus is shown

in the chest. These are present in varying degrees and combinations, depending on the site and degree of the encroachment on the pleural cavity, or they may not be present at all. The abdominal symptoms are caused by incarceration of the abdominal viscera in the hernial opening, this causes disturbance of the function of the organs involved, varying from slight irritation to strangulation and obstruction.

Morrison<sup>9</sup> states that the most constant symptom is pain just above or anterior to the ensiform cartilage. The symptoms often simulate irregularly those of peptic ulcer or cholecystitis with hemorrhage, or pain radiating to back or left shoulder, gastric distress, palpitation at night and inability to lie on the back or left side without regurgitation of acid fluid. He states that all but one of his forty-two cases had been

12 Lacher, quoted by Unger and Speiser. *Am J Roentgenol* 15 135 1926

# PRELIMINARY MEDICATION IN GENERAL ANESTHESIA

WITH SPECIAL REFERENCE TO THE MARGIN OF SAFETY AND  
POSTOPERATIVE LESIONS OF THE LUNG

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AND

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The reasons for giving preliminary medication are to prevent psychic shock, to increase the margin of safety, to modify or abolish any and all untoward symptoms during induction and maintenance of anesthesia and after operation, and, most important of all, to prevent possible pathologic lesions in the lungs. Preliminary medication should be given regardless of whether the anesthesia is local, spinal, regional or general. In the search for a suitable agent for preliminary medication, magnesium sulphate should be considered. It synergizes with morphine by prolonging its effect, and if ether is used, the magnesium sulphate deepens the anesthesia.

Table 1 is a summary of cases from more than 200 similar cases selected in sequence at the Presbyterian Hospital of New York City in which 400 cc of a sterile 4 per cent chemically pure magnesium sulphate solution (4 drachms [15.5 Gm] of the salt) was given by hypodermoclysis one and a half hours before operation<sup>1</sup>. Three eighths of a grain (24 mg) of morphine in divided doses was given by hypodermic injection. When magnesium sulphate was used, the average time after operation before a sedative was required was sixteen hours. Table 2 shows a parallel series of cases in which morphine alone was given. The average time after operation that a sedative was given was four hours.

Table 3 shows a second series of cases, in sequence, from another hospital in which 6 cc of 25 per cent solution of magnesium sulphate divided into three doses, each dose containing one eighth of a grain (8 mg) of morphine sulphate, was injected intramuscularly as preliminary medication to nitrous oxide-oxygen and procaine anesthesia. The gases are used only to render the patient unconscious and to complete the analgesia. The patient remains pink, and the usual signs of third stage anesthesia are not present. Table 4 gives the results in a parallel series of cases in which morphine dissolved in water was given. The results in each hos-

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1 Gwathmey, J. T., and Greenough, James. Synergistic Analgesia with Nitrous Oxide—Oxygen and Magnesium Sulphate, *M. Rec.* **100** 583 (Oct 1) 1921.

after meals, (2) inability to take quantities of food, (3) a sense of smothering or distress and (4) inability to vomit or belch gas during an attack (figs 2 and 3)

The most constant symptom in the surgical cases at the Mayo Clinic was epigastric pain, it was noted in practically all cases. In four cases it radiated to the thorax anteriorly, in three cases to the back, and in two



Fig 5—Left diaphragmatic hernia, abdominal left rectus incision, almost the entire stomach in the left thoracic cavity, a portion of transverse colon and spleen having been removed from the cavity. Insert *a* shows hernial opening to left of esophageal opening with large cavity in the left lower thorax. Insert *b* shows closure of hernial opening with interrupted catgut reinforced with linen sutures after a phrenic neurectomy.

cases to the left shoulder. The other symptoms in order of frequency were regurgitation of sour fluid or food, vomiting, gastric distress and distention with difficulty in belching of gas at times, distress immediately after eating, hemoptysis and melena.



TABLE 3—*Patients Receiving Magnesium Sulphate and Morphine*

Number	Operation	Time of Postoperative Sedative
1	Colpoperineorrhaphy	None
2	Appendectomy and cholecystectomy	None
3	Appendectomy	12 hours
4	Appendectomy and cholecystectomy	3 hours
5	Appendectomy	10 hours
6	Perineorrhaphy	12 hours
7	Cholecystectomy	16 hours
8	Hysterectomy and double oophorectomy	9 hours
9	Secondary closure	None
10	Nephrectomy	23 hours
11	Hysterectomy	None
12	Perineorrhaphy, appendectomy, ventrosuspension	5 hours
13	Appendectomy	None
14	Appendectomy	None
15	Appendectomy and cholecystectomy	24 hours
16	Appendectomy and Cobbett's cyst	12 hours
17	Radical amputation of the breast	None
18	Appendectomy and Schroeder's operation	12 hours
19	Appendectomy	4 hours
20	Schroeder's operation	None
21	Perineorrhaphy	4 hours
22	Hysterectomy, colporrhaphy, perineorrhaphy	17 hours
23	Appendectomy and cholecystectomy	12 hours
24	Appendectomy and dilatation of cervix	None
25	Appendectomy and cholecystectomy	23 hours
26	Separation of adhesions, omental graft under liver	6 hours
27	Barrett's operation, separation of adhesions	33 hours
Total lapse of time before postoperative sedative		256 hours
Average lapse of time		15 hours

TABLE 4—*Parallel Series of Cases in Which Magnesium Sulphate Was Not Given*

Number	Operation	Time of Postoperative Sedative
1	Cholecystectomy	12 hours
2	Cholecystectomy	8 hours
3	Cholecystectomy	4 hours
4	Cholecystectomy	2 hours
5	Appendectomy	12 hours
6	Appendectomy	3 hours
7	Appendectomy	1 hour
8	Appendectomy	None
9	Appendectomy	1 hour
10	Drainage of appendix	2 hours
11	Freeing stricture	2 hours
12	Freeing stricture	1 hour
13	Gastro-enterostomy, appendectomy	3 hours
14	Freeing adhesions	12 hours
15	Repair of hernia	2 hours
16	Radical cure of hernia	None
17	Herniotomy	11 hours
18	Herniotomy	None
19	Removal of appendix, ovary, tubes and uterus	1 hour
20	Hysterectomy	12 hours
21	Hysterectomy	None
22	Hysterectomy	2 hours
23	Hysterectomy	2 hours
24	Hysterectomy	8 hours
25	Hysterectomy	7 hours
26	Cesarean section	4 hours
27	Cesarean section	3 hours
Total lapse of time before postoperative sedative		110 hours
Average lapse of time		4 hours plus



Fig 7—Traumatic diaphragmatic hernia following gunshot wound The bullet is seen in the left flank at the level of the eleventh rib The entire stomach was below the diaphragm after operation

safer agent Acetylene has passed the experimental stage, having been used in thousands of cases in Germany<sup>6</sup> Propylene is still in the experimental stage and should not be used clinically at this time The best results with these agents are obtained by using nitrous oxide and ethylene in combination, nitrous oxide and oxygen should be used at first and ethylene should be added when unconsciousness ensues The anesthetic is then continued with nitrous oxide, oxygen and ethylene

In regard to immediate safety for life, ether has a wider margin than any of the gases described Its use is increased in value by premedication more than any other general anesthetic, as the following experiments show<sup>7</sup>

#### REPORT OF EXPERIMENTS

*Without Preliminary Medication*—On June 15, 1915, at 10 30 a m, a dog weighing 13 Kg was given 0.5 cc of 2 per cent morphine solution At 11 34, intravenous administration of ether was started At 11 38½, complete anes-

TABLE 5—*Comparison of Analgesic and Anesthetic Doses of Propylene, Acetylene, Ethylene and Nitrous Oxide, With and Without Preliminary Medication*

Cases	Results Obtained			
	With Preliminary Medication		Without Preliminary Medication	
	Complete Analgesia, Percentage of Anesthetic Gas	Anesthesia, Percentage of Anesthetic Gas	Complete Analgesia, Percentage of Anesthetic Gas	Anesthesia, Percentage of Anesthetic Gas
Propylene-oxygen	28	50	50	50
Propylene air	36	46	46	46
Acetylene-oxygen	41	41	75	75
Ethylene-oxygen	73	92	87	94
Nitrous oxygen	91	93	93	93

thesia was obtained by the use of 134 cc of ether solution At 11 42, respiratory failure occurred, only 99 cc more of the ether solution was required

The animal was then resuscitated by artificial respiration A period varying from four to seven days or more was allowed for recovery After this rest, the experiment was repeated as follows

*With Preliminary Medication*—On Sept 7, 1915, at 2 50 p m, 0.5 cc of 2 per cent morphine solution was given At 3 10, 6.05 cc of paraldehyde and 13 Gm of potassium bromide were given At 3 59, intravenous administration of ether was started At 4 01½, complete anesthesia was obtained, using 87 cc of ether solution At 4 09½, respiratory failure occurred, 245 cc more ether solution was required

In both experiments the dog received sufficient morphine to make him easy to handle, so this factor can be excluded from the final result Without pre-

6 Gwathmey, J T Ethylene and Preliminary Medication, Arch Surg 10 568 (Jan) 1925

7 Gwathmey, J T Anesthesia Reviewed, New York M J 104 825 (Oct 28) 1916, 104 895 (Nov 4) 1916

of the herniated abdominal viscera, operation is usually indicated. In acute cases due to penetrating wounds with rupture of a viscus, immediate operation is demanded. In acute cases due to indirect injury of the diaphragm without injury to the viscera, palliative measures are probably preferable until the shock of injury and the acute symptoms subside. Gastric lavage is often of great assistance in relieving the acute gastric symptoms. Placing the patient in Fowler's position often relieves the respiratory embarrassment. Stimson<sup>15</sup> stated that induction of artificial pneumothorax before operation may reduce the shock and

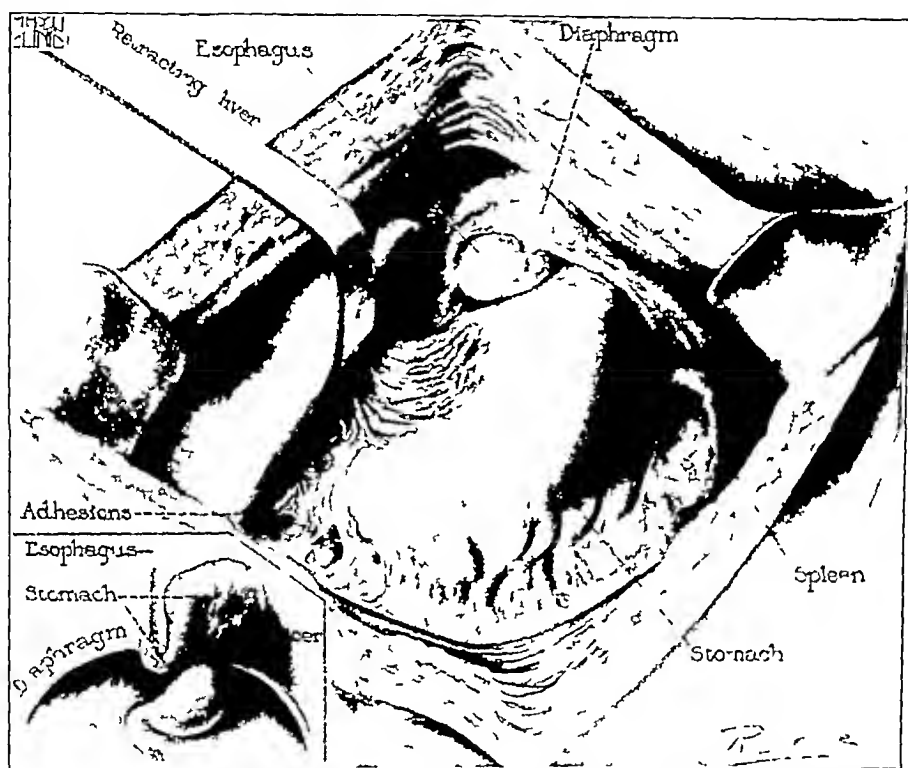


Fig 9—High right rectus incision, one third of the stomach herniating through esophageal opening of diaphragm. Many adhesions of the pyloric end of the stomach to under surface of the liver, due to a previous operation on the gall-bladder. The insert shows a diagrammatic sketch of the portion of the stomach above the diaphragm, containing ulcer.

aid in the reduction of the hernia. The patient should be so placed on the operating table that the abdominal viscera gravitate toward the pelvis. I prefer a semi-upright position with the head and thorax tilted well back.

The method of approach may be thoracic or abdominal or a combination of the two. In the twenty-seven surgical cases, all three methods

<sup>15</sup> Stimson, P. M. Congenital Diaphragmatic Hernia of the Right Side its Diagnosis in life, *Arch. Pediat.* 40: 647, 1923.

The albino rats employed were obtained from one source and were kept on a constant, well balanced diet for at least two weeks before the tests were made. After fasting for from sixteen to twenty hours immediately before the experiments, they were weighed and the preliminary medication injected, the dosage being computed on the basis of kilograms of body weight. Water was supplied during the fasting period.

Four animals were employed for each experiment. Two were given intramuscular injections of 0.8 cc of magnesium sulphate solution (50 per cent) per kilogram of body weight with procaine hydrochloride (2.5 per cent) and morphine sulphate ( $\frac{1}{8}$  grain in 2 cc). Ten minutes after the preliminary injections, all four animals were placed in the gas chamber and were given the same mixture with the gages set, so that all were killed within thirty minutes. The controls jumped around and struggled against the anesthetic. The animals receiving the preliminary medication fell asleep without going through a stage of excitement. After the animals were killed with the anesthetic mixtures, necropsy was immediately performed. Lesions in the lungs occurred in the ones that did not receive preliminary medication, gross examination showed distention, edema and congestion. After ether was used, it was not unusual to find atelectasis involving one or more of the lobes. The lungs of the animals that received preliminary medication were relatively normal. Illustrations of this condition are given in Nelson's Loose Leaf Surgery.<sup>9</sup>

#### CONCLUSIONS

The preliminary medication suggested for clinical purposes is an injection of morphine sulphate, one-eighth grain dissolved in 2 cc of magnesium sulphate solution (50 per cent). This is to be repeated once or twice at twenty or thirty minute intervals, according to the age, weight and general condition of the patient. If an idiosyncrasy is present, it will develop before the time for the third dose. One fourth of a grain of morphine is usually sufficient for women.

If the patient is to be put to sleep entirely, we give, in addition to the hypodermic injections, a small dose of ether,  $2\frac{1}{2}$  ounces (14.2 cc), by rectum, paraldehyde, 2 drachms (7.8 Gm) and olive oil, sufficient to make 4 ounces (118.4 cc). Any nurse can give this retention enema, and the procedure does not require an anesthetist, as surgical anesthesia would never be induced by this medication. If nitrous oxide and oxygen are used, the oxygen should be increased to 30 or 50 per cent, instead of the usual 9 or 10 per cent. If procaine hydrochloride is used for the skin and the peritoneum, the same percentage is required as would be used if preliminary medication had not been given. If chloroform and ether are used, only a few drops are required.

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<sup>9</sup> Nelson's Loose Leaf Surgery, vol 9, opposite p 514

